DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2010

THURSDAY, MAY 21, 2009

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 10:29 a.m., in room SD–138, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin and Shelby.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF RAYNARD S. KINGTON, M.D., PH.D., ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH

ACCOMPANIED BY:

JOHN E. NIEDERHUBER, M.D., DIRECTOR, NATIONAL CANCER INSTITUTE

ELIZABETH G. NABEL, M.D., NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. Good morning. The Subcommittee on Labor, Health, Human Services, and Education will come to order.

This morning we will examine the President's proposed fiscal year 2010 budget for the National Institutes of Health (NIH). We'll also discuss the $10.4 billion that was provided for NIH in the Recovery Act.

I would say at the outset these are exciting times for NIH. After several years of stagnant funding, the Recovery Act has breathed new life into the field of biomedical research. The new Challenge Grant Program alone has generated more than 20,000 applications from researchers across the country, far more than anyone expected.

The scientific advances that result from this funding will probably take some time to gauge but in the meantime, I expect it to have a tremendous impact on the economy. Every time a researcher gets a grant, it supports an average of six or seven jobs. That's not just one researcher by himself or herself. It's lab techni-

cians, post-doc fellows and research assistants, and then there's the ripple effect of the research itself.

Maybe this grant leads to a new compound that a pharmaceutical company wants to develop into a new drug and that means more money in our economy. Maybe an entrepreneur uses some breakthrough to form a spin-off company. That stimulates the economy, also.

I just want to note for the record, I don't want any of you here at the table to take this wrongly, but all of this money won't just go to Bethesda. It goes to researchers in every State and it helps the entire country.

But while there's a great deal of optimism about the next 2 years, there's also a concern about what happens after the Recovery Act funding runs out in the year 2011. After 2 years of healthy budgets, will we then have a cliff effect where we just kind of fall again?

That's one of the questions I will want to discuss with our witnesses today.

At this point, I know Senator Cochran is also on our Defense Committee hearing mark-up and will probably be here later, but I'll leave the record open for his opening statement at this point and any other statements that any members of the subcommittee might have.

This morning we have Dr. Raynard S. Kington who was named Acting Director of the National Institutes of Health on October 31 of last year, before that he was Deputy Director for 5 years under Dr. Zerhouni.

Dr. Kington received his B.S. and M.D. degrees from the University of Michigan and a Ph.D. from the University of Pennsylvania, and I just want to add that, Dr. Kington, I know you've served in this capacity probably longer than you thought you were going to have to serve. But by every account that I have seen, you have done a great job in running this agency and I just want to thank you for this period of service and for all the previous service, Dr. Kington.

Also at the table is Dr. Anthony Fauci, the Director of the National Institute of Allergy and Infectious Diseases. Again, I don't know if you've ever kept count of how many times have you appeared before this subcommittee, Tony, going back all these years? But again, welcome.

Dr. Fauci came to NIH in 1968, after completing his residency at the New York Hospital, Cornell Medical Center. He received his M.D. degree from Cornell University Medical College.

Dr. Elizabeth Nabel is the Director of the National Heart, Lung, and Blood Institute, appointed to that position in 2005, received her M.D. from Cornell University Medical College, and prior to coming to NIH, Dr. Nabel was the Chief of Cardiology and Director of the Cardiovascular Research Center at the University of Michigan.

Dr. John Niederhuber is the Director of the National Cancer Institute, a graduate of Bethany College in West Virginia, received his medical degree from Ohio State, and prior to coming to NIH, Dr. Niederhuber was a Professor of Surgery and Oncology at the University of Wisconsin School of Medicine.

I know other Directors are here this morning. Dr. Lawrence Tabak at the National Institute of Dental and Craniofacial Research is here. Dr. Tabak is here.

Dr. John Ruffin from the National Center on Minority Health and Health Disparities.

Dr. Steven Katz, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, Dr. Katz is here, yes.

Dr. Story Landis of the National Institute of Neurological Diseases and Stroke, Dr. Landis.

Dr. Richard Hodes, National Institute of Aging. Nice to see you again.

Dr. Griffin Rodgers from the National Institute of Diabetes and Digestive and Kidney Diseases, NIDDK.

And Dr. Thomas Insel, National Institute of Mental Health, also here, too.

Thank you all for being here.

Now, I had a series of really wonderful hearings last year where we brought down something like three directors at a time, and I wanted to do that this year, but because of healthcare reform that we're working on and I also wear another hat, we're trying to get the reauthorization of the Child Nutrition bill through, so there's just a lot of things piled up on us right now, so I don't have that luxury.

I think it's very important that we hear from the Directors of these Institutes in a more indepth session. I will just say, Dr. Kington, it's my intent, consistent with what we have to do here in the Senate this year, that maybe we can catch up on this later on. I'm still hopeful that maybe this fall some time, if we get our healthcare reform bill through and we have a little bit more time I would come back and hopefully revisit that and reprise what we did again last year.

I just don't have the time to do it now, but sometime this fall. So I say to you and the other directors it is my intent to do that. Okay?

Well, with that, Dr. Kington, we'll turn to you for your statement. I just would say that all of your statements will be made a part of the record in their entirety and if you'd just summarize them in 5 minutes or so, I'd certainly appreciate it.

Dr. Kington.

SUMMARY STATEMENT OF DR. RAYNARD S. KINGTON

Dr. KINGTON. Thank you. Mr. Chairman, it's a privilege to appear before you today to present the National Institutes of Health budget request and to discuss the priorities of NIH for fiscal year 2010 and beyond.

Again, I would like to thank all of my colleagues whom you've noted who are here joining me today and we would welcome the opportunity to come back and have further discussions whenever it is convenient.

First, I want to express my gratitude to Congress and the president for the support reflected in the recent appropriation of $10.4 billion in the American Recovery and Reinvestment Act (ARRA) for NIH expenditure and the 3.2 percent increase in the annual fiscal year 2009 appropriations for NIH.

The continued trust that you place in the NIH to make the discoveries that will lead to better health for everyone is appreciated.

I thank you on behalf of the many scientists who we are able to support and more than 3,000 research institutions throughout the United States and on behalf of the public who count on our research to help detect, treat and prevent hundreds of diseases and conditions.

As noted, I have submitted my testimony for the record and will just highlight key points for you now.

FISCAL YEAR 2010 BUDGET REQUEST

The budget request embodies the President's fundamental goal of increasing overall Federal investment in biomedical research as well as the President's particular emphasis on accelerating research in the areas of cancer and autism in fiscal year 2010.

The budget request provides $31 billion, an increase of $443 million or 1.4 percent over fiscal year 2009, to help fill in gaps in our fundamental understanding of health and disease. This request will increase funding for research project grants by $243 million.

The request supports an estimated 9,849 new and competing research project grants, about the same level as in fiscal year 2009, which will provide a success rate in 2010 of about 20 percent.

The fiscal year 2010 President's budget request includes the following priorities. For cancer research, an increase of investment across the NIH to over $6 billion reflecting the first year of an 8-year strategy to double cancer research by fiscal year 2017. This request represents an increase of $268 million or 5 percent over an estimated fiscal year 2009.

For autism research, the NIH will contribute $141 million of the $211 million department-wide initiative on autism. Working with the Centers for Disease Control and Prevention and the Health Resources Service Administration, we will use these funds to support research into the causes of and treatment for autism spectrum disorders. For NIH this represents an increase of $19 million or about 16 percent above the estimated fiscal year 2009 level.

ECONOMIC AND SCIENTIFIC BENEFITS OF ARRA

I expressed earlier my gratitude to the President and Congress for their support of the NIH with ARRA. It is time that the ARRA funds be provided to NIH to stimulate the economy and advance biomedical and behavioral research. The biomedical research community is not spared from the recent downturn in the economy. This is worrisome not only because it means fewer jobs but also because innovation and a constant influx of young talent are crucial to the Nation's economic success and a robust biomedical research enterprise.

We are moving quickly to identify the best science and support it with an additional $10.4 billion provided by ARRA to NIH and to obligate it within the next 2 years. We have already started selecting projects to receive the funding. To date NIH has begun obligating more than $375 million worth of ARRA support to a wide array of important projects. We expect the number of actions to increase exponentially over the coming weeks and months.

For example, NIH ARRA funding is already supporting research to construct a reference sequence dataset for the Human Microbiome Project. This genomic survey project promises to lay the foundation for future advances to understand the impact that microbes in the human body have on health and disease.

Another funded project seeks to develop molecular targeting to improve the delivery and efficacy of treatments for deadly brain tumors known as glial blastomas.

Still another ARRA grant will support a Pittsburgh lab that has been developing a minimally invasive surgical approach for removing intracerebral hematomas, deadly bruises on the brain. In this case ARRA funds have allowed the lab to reopen and the staff newly returned to their benches to continue their potentially life-saving studies.

Furthermore, your funding decisions sent a strong message to scientists in the field and to bright young people who may one day choose a career as scientists that the United States is working to support outstanding research and outstanding scientists.

Just yesterday the Baltimore Sun published a story on the impact of ARRA funding and here's a quote from the article.

"There are a lot of really good ideas that were dying on the vine because they weren't getting funding," said James Hughes, Vice President for Research and Development at the University of Maryland, Baltimore, "but with the stimulus money, Hughes estimates that his medical, pharmacy, dental, and nursing schools could see as much as an additional $100 million over the next 2 years, money that will not only further research but would create hundreds of good jobs."

I am certain that similar scenarios are occurring throughout the country and will continue to do so over the next 2 years as we implement this act. Here's only a sampling of the important work that we will support with the ARRA funds.

For example, we will expand our current understanding of a wide array of diseases and conditions, including diabetes, various forms of cancer, addiction, glaucoma, infectious diseases, heart and lung diseases, arthritis, kidney disease and mental disorders.

In addition, we will expand our efforts in community-based research with special focus on minority and under-served populations, and make further investments into the potential applications of nano technology.

Just to review briefly, the ARRA funding to NIH will be used in the following ways. The legislation allocated $1.3 billion for the National Center for Research Resources with $1 billion identified for extramural construction and renovation and $300 million targeted for shared instrumentation and other large capital research equipment.

The positive impact of the support for institutions and researchers will be extraordinary, providing broader access to the state of our equipment. Funding for extramural construction and renovation will result in jobs in construction and a number of trades in the building industry.

Shared instrumentation will improve the quality and even the speed of work that is done and build collaboration in ways that will accelerate discovery. Shared scientific instrumentation, including such resources as advanced real-time imaging tools, will allow sci-

entists to image the brain in action in ways that have not been possible before.

You appropriated $8.2 billion to NIH, of which $7.4 billion was distributed through the Office of the Director to Institutes and Centers of NIH and to the common fund for the direct support of biomedical research. The remaining $800 million was distributed by the Office of the Director to fund specific research challenges of scientific priorities at the Institutes and Centers.

Our current projections are that NIH activities with these funds will support more than 7,000 new awards, most of which will be for 2 years of scientific research.

In addition, $400 million transferred to NIH from the Agency for Healthcare Research and Quality as directed under ARRA and will be used to support comparative effectiveness research. The remaining $500 million will be used to fund high-priority repairs, improvements, and construction on the NIH Bethesda campus to enable the highest-quality research to be conducted.

Let me review how NIH will be using ARRA dollars in direct support of science.

NIH developed a nimble approach to investing the money quickly and with the greatest impact. For example, we are in the process of scrutinizing approximately 14,000 grant applications we received in our last round of review, applications that were already highly meritorious and approved by advisory councils at each Institute and Center, applications that despite their merit we could not fund before.

We are now identifying and planning to fund some of these scientifically meritorious applications for 2 years where the scientific plan is appropriate for a 2-year award instead of the usual 4-year award.

NIH has already issued a number of new funding announcements. In particular, we've made targeted grant announcements to stimulate research in high-priority exempt areas. An excellent example is research funding opportunities related to autism, a disease that affects so many families across the United States.

NIH has committed $60 million of research funding, in addition to a $141 million in the base budget request, to address the differences across autism spectrum disorders. Resources will help develop and test diagnostic screening tools, assess risk for exposures, test early interventions and adapt existing pediatric treatments for older groups with autism spectrum disorders.

While few trials can be completed in 2 years, the ARRA funds will be important for jumpstarting projects and building the foundation for longer-term autism research.

NIH has created a number of new programs that will spur new areas of research and trigger an almost immediate influx of research dollars into communities across the Nation.

For example, we've introduced the Challenge Grants, the Grant Opportunity or GO Grants, Signature Initiatives, a program to encourage the recruitment of new faculty to conduct research, and a program to hire students and science teachers to work in research laboratories.

For the Challenge Grants, we issued the largest request for applications in NIH history, which is saying something, to initiate the

program. The 220-page solicitation lists 237 scientific topics in 15 broad scientific areas. As noted, we initially expected to devote approximately $200 million to this effort, funding the best proposals from a pool of around 15,000, we initially estimated. However, upon receiving well over 20,000 applications, we now anticipate devoting substantially more than that.

The magnitude of the response demonstrates the breadth and depth of the scientific capacity that exists across the United States, capacity awaiting only financial support to be actualized. It is inspiring to witness the scope and creativity of American scientists.

Here are only a few examples of Challenge Grant topics. New advances in biosensors and lab on a chip technology to create novel ways to measure the health effects of contaminants in the environment and develop high-tech blood and tissue analysis techniques, new approaches to better understand persistent HIV–1 infections in patients receiving antiretroviral therapy, and enhancing research in the bioethics field.

Another new program is the Grant Opportunity Program or GO Grants. The GO Grant Program which was designed to complement the Challenge Grants will support large-scale research projects. These large-scale projects will accelerate critical breakthroughs early in applied research on cutting edge technologies and new approaches to improve the interactions among multidisciplinary, interdisciplinary research teams. The applications are due on May 29th of this year and I know that we've received already more than 2,400 letters of intent from potential applicants.

NIH is also identifying a number of Signature Initiatives that will support exceptionally creative and innovative projects and programs to address major challenges in biomedical research in public health. The initiatives will cover new scientific opportunities in nano technology, genome-wide association studies, health disparities, arthritis, diabetes, autism, genetic risk for Alzheimer's disease, regenerative medicine, oral fluids as biomarkers, and HIV vaccine research.

In addition to direct support from the Institutes and Centers ARRA funds, the Office of The Director will also support at least $30 million from its ARRA funds for these signature projects.

We've also announced a new program to support newly trained faculty to conduct research. This will help address the need to support early career scientists who are one of NIH's top priorities. Funding will be provided to hire, provide appropriate start-up packages, and develop pilot research projects for newly independent investigators. The applications for this program are due to NIH May 29, as well.

We are particularly delighted to tell you about our expanded summer program for teachers and students from all 50 States and the District of Columbia. NIH will use $35 million of ARRA dollars to support short-term jobs over 2 summers for over 3,700 individuals. Most of these will be high school and undergraduate students, though the number also includes several hundred elementary, middle, high school, and community college science educators.

This laboratory experience around the country will provide several thousand Americans with the opportunity to experience the ex-

traordinary world of research. We hope this experience will spark the desire of many of these students to become scientists.

We are mindful that a top priority for the use of ARRA funds by NIH is to create and preserve jobs as well as to increase purchasing power in all corners of the country. We firmly believe that we can do this while carrying out the core NIH mission and without compromising our commitment to fund the very best scientific research ideas.

We will fulfill ARRA's comprehensive reporting requirements, including jobs created and preserved, tracking of all projects and activities and trend analysis. To track all of the NIH ARRA-related activities, I invite you to go to our Web site, www.nih.gov, which we will update regularly.

In summary, groundbreaking discoveries are most often built on the foundation of many incremental advances that bring us closer to early diagnoses, better treatments and other public health improvements expected by Congress and the American public.

Because of the ARRA funds, there will be more discoveries across the country next year and many years thereafter. These findings will yield better understanding of the major diseases and disorders, including those I touched on today, and hundreds more, as well as providing keys to living healthier lives.

As I said in my opening comments, we are grateful for the commitment to biomedical research and all the promise it brings to the people here in the United States and around the world. We have employed a number of innovative strategies to quickly and wisely invest ARRA funds. We still stimulate the economy, create jobs and advance science.

Most importantly, however, ARRA will help contribute to our principal mission: to make scientific discoveries that will improve people's health.

PREPARED STATEMENTS

I will be pleased to answer any questions that you might have.
[The statements follow:]

PREPARED STATEMENT OF RAYNARD S. KINGTON

Good morning, Mr. Chairman and distinguished members of the subcommittee.

It is a privilege for me to appear before you today to present the National Institutes of Health (NIH) budget request and to discuss the priorities of NIH for fiscal year 2010 and beyond.

First, I want to express our gratitude for your and the President's support as reflected in the recent appropriation of $10.4 billion in the American Recovery and Reinvestment Act (ARRA) for NIH expenditure and the 3.2 percent increase in annual fiscal year 2009 appropriations for NIH. The continued trust that you place in NIH to make the discoveries that will lead to better health for everyone is appreciated.

I thank you on behalf of the many scientists we are able to support at more than 3,000 research institutions throughout the 50 States and United States territories; and on behalf of the public, who count on our research to help detect, treat, or prevent hundreds of diseases and conditions.

As you well know, research conducted and supported by the NIH touches people's lives every day. NIH is the largest single engine for outstanding biomedical research in this country—and the world. Not only does NIH have an impact globally, it also has a lasting impact at the community level, bringing intellectual and economic growth to towns and cities across America.

Fiscal Year 2010 Budget Request

The budget request embodies the President's fundamental goal of increasing overall Federal investment in basic research and development as well as particular emphasis on accelerating research in the areas of cancer and autism in fiscal year 2010.

The budget request provides $31 billion, an increase of $443 million or 1.4 percent over fiscal year 2009, to help fill gaps in our fundamental understanding of health and disease. NIH Research Project Grants (RPGs) support scientists to discover the fundamental underpinnings of complex human biology through investigator-initiated research, the mainstay of creativity in science. This request will increase funding for RPGs by $243 million. The request supports an estimated 9,849 new and competing RPGs, about the same level as fiscal year 2009.

The fiscal year 2010 President's budget request includes the following priorities:

Cancer Research.—Increases the investment across NIH to over $6 billion for cancer research across NIH, reflecting the first year of an 8-year strategy to double cancer research by fiscal year 2017. The fiscal year 2010 request represents an increase of $268 million or 5 percent over the estimated fiscal year 2009 level.

Autism Research.—Invests $141 million of the $211 million Department-wide initiative on autism. This total amount includes the Centers for Disease Control and Prevention and Health Resources Services Administration for research into the causes of and treatments for autism spectrum disorders. For NIH, this represents an increase of $19 million or 16 percent above the estimated fiscal year 2009 level.

Economic and Scientific Benefits of ARRA

I expressed earlier my gratitude to the President and Congress for their support of NIH with ARRA. It is timely that ARRA funds be provided to the NIH to stimulate the economy and advance biomedical and behavioral research. The biomedical research community has not been spared from the drastic downturn in the economy. This is worrisome not only because it means fewer jobs, but also because innovation and a constant influx of young talent are crucial to the Nation's economic success and a robust biomedical research enterprise.

We are moving quickly to identify the best science and support it with the additional $10.4 billion provided by ARRA to the NIH, and obligate it within the next 2 years. Moreover, your decision sends a strong signal to the scientists in the field, and to bright young people who may one day choose science as a career, that the United States is working to support outstanding research and outstanding scientists.

To demonstrate the impact ARRA will have at the individual level, I would like to share with you the following: One of our program directors received an email after enactment of ARRA in response to news that an applicant's grant application was being considered for funding with ARRA money.

Here is an excerpt from the email (with names deleted):

"Forgot to say that we gave a termination letter last Friday to my longtime (5 years) postdoc. His job has been saved. He is going to be thrilled to hear about his change in fortune! I also would like to hire a technician with the new funds, since at present I do not have one."

Let me highlight some of the important work that we will support with ARRA funds. For example, we will rapidly expand our current understanding of the genetic changes associated with a wide range of diseases and conditions, including addiction, Alzheimer's disease, various forms of cancer, chronic pain, diabetes, glaucoma, heart and lung diseases, kidney disease, and mental disorders, through genetic analysis of existing, well characterized population cohorts. We will take steps toward using this genetic information to better inform the modification of disease for those patients most at risk, principally through lifestyle factors and personal health behaviors.

In addition, our efforts to expand community-based research efforts, with special focus on minority and underserved patients, will be accelerated through catalytic grants designed to enhance interrelationships among academic health centers, community organizations, and community healthcare clinical centers. Evaluation of the health and safety risks of nanoscale products is critical as nanomaterials are being used in applications as diverse as medical devices, drug delivery, cosmetics, and textiles. Biological, physical, and chemical characterization of selected nanomaterials will be conducted to both inform the establishment of standards for health and safety and developing computational models for the prediction of long-term secondary effects.

Just to review briefly, the ARRA provided NIH funding in the following ways:

—It allocated $1.3 billion for the National Center for Research Resources, with $1 billion identified for extramural construction and renovation, and $300 million targeted for shared instrumentation and other large capital research equipment. The positive impact of this support for institutions and researchers will be extraordinary, providing broader access to state-of-the-art equipment. Funding for extramural construction and renovation will result in jobs in construction and a number of trades in the building industry. Shared instrumentation will improve the quality and even the speed of the work that is done, and build collaboration in ways that will accelerate discovery. Shared instrumentation, including such resources as advanced real-time imaging tools, will allow scientists to image the brain in action or enable them to see separate proteins that play a role in health and disease.

—It appropriated $8.2 billion to NIH, of which $7.4 billion will be distributed through the NIH Office of the Director, to the Institutes and Centers of NIH, and to the common fund for the support of biomedical research. The remaining $800 million will be distributed by the Office of the Director to fund specific challenges and scientific priorities at the Institutes and Centers.

—In addition, $400 million transferred to NIH by the Agency for Healthcare Research and Quality (AHRQ), as directed under ARRA, will be used to support comparative effectiveness research.

—The remaining $500 million will be used to fund high-priority repairs, improvements, and construction on the NIH campus to enable the highest quality research to be conducted.

How Will NIH Accomplish This Task

NIH is determined to seize the opportunity afforded by the infusion of ARRA resources to develop a nimble approach to investing the money quickly with the greatest impact. This opportunity is too important for us to conduct "business as usual." It demands that we employ the best possible approaches to ensure progress at in an accelerated pace, with the most efficient and effective use of resources. For example, we are scrutinizing the 14,000 grant applications we received in our last round of review—applications that were already deemed highly meritorious and approved by Advisory Councils at each Institute and Center—applications that, despite their merit, we could not fund before. We are now starting to fund those scientifically meritorious applications for 2 years, where the scientific plan is appropriate for a 2-year award instead of the usual 4-year award. Also, every Institute and Center is identifying scientific priorities that can be funded through administrative supplements. Administrative supplements will accelerate the progress of a promising grant, typically by adding support for postdoctoral scientists and graduate students and key pieces of equipment

The NIH team is proud of the trust placed in it to be a part of the economic recovery process. NIH will work tirelessly to support the goals and intent of ARRA, with wise resource investments in science.

NIH has created a number of new programs that will spur new areas of research and trigger an almost immediate influx of research dollars into communities across the Nation. For example, NIH created a new program called the Challenge Grant award. To jump start this program, we issued the largest Request for Applications in our history. This 220-page document lists numerous scientific topics in 15 broad scientific areas, including: bioethics, translational science, genomics, health disparities, enhancing clinical trials, behavioral change and prevention, and regenerative medicine—areas that would benefit from a jumpstart or in which a scientific challenge needs to be overcome. The Office of the Director expects to devote at least $200 million of these funds to this effort.

I will highlight only a few examples of the Challenge Grant topics that could be further explored:

—New advances in biosensors and lab-on-chip technology to create novel ways to measure the body burden and sub-clinical health effects of emerging contaminants in the environment in large study populations. Additional research funds could support field testing of the most promising sensors and analysis techniques through collaboration with existing epidemiologic studies taking advantage of both new and banked tissue specimens.

—There is increasing evidence that suggests that HIV–1 infected individuals experience similar immunologic changes as the uninfected elderly. This may be due to persistent stimulation of the immune cells. It is not clear whether antiretroviral therapy can reverse this process. Research will aim to compare the effectiveness of different treatment regimens in reversing or preventing accelerated aging that appears in the immune and other body systems.

—Studies are needed to assess the impact and ethical considerations of conducting biomedical and clinical research internationally in resource-limited countries.

Another new program is what we call the Grand Opportunity Program, or "GO grants." The purpose of this program is to support high-impact ideas that require significant resources for a discrete period of time to lay the foundation for new fields of investigation. The GO program will support large-scale research projects that accelerate critical breakthroughs, early and applied research on cutting-edge technologies, and new approaches to improve the synergy and interactions among multidisciplinary and interdisciplinary research teams. Applicants may propose to address either a specific research question or propose the creation of a unique infrastructure/resource designed to accelerate scientific progress. For those projects that span the missions of multiple Institutes, Centers, and Offices (ICs), support may come from ARRA funds allocated to the Common Fund.

NIH will identify a number of signature initiatives that will support exceptionally creative and innovative projects and programs—and potentially transformative approaches to major challenges in biomedical research. The initiatives will cover new scientific opportunities in nanotechnology, genome-wide association studies, health disparities, arthritis, diabetes, autism, and the genetic risk for Alzheimer's disease, regenerative medicine, oral fluids as biomarkers, and HIV vaccine research.

Each IC is developing at least one signature initiative, and a number will be done in partnership across ICs and/or the Office of the NIH Director. The areas being developed include an Office of the Director-led set of catalytic awards to enhance community-based research efforts to ensure that we are able to reach segments of our Nation that are too often overlooked in clinical research.

In addition, considerable investment is expected to be made to understand the genetics of a wide range of specific diseases and conditions, as well as second generation "deep DNA sequencing" of very large and well-defined national patient cohorts to identify disease causing genetic variants. Using new technology developed with NIH-support, "deep sequencing" allows analysis of genome sequence from many individuals to provide greater insight about subtle genetic variations than could previous methods, and does so at lower cost." An initiative to modify disease risk-based on genome-wide association findings is also being planned. Complementing this will be initiatives to accelerate biomarker discovery and validation.

Also, NIH will use other funding mechanisms, such as the Academic Research Enhancement Award, or AREA grants, that support small research projects in the biomedical and behavioral sciences conducted by faculty and students in health professional schools and other academic components that have not been major recipients of NIH research grant funds. A research program to support new faculty, called the "Core Centers for Enhancing Research Capacity in U.S. Academic Institutions," will address the need for more bioethicists and provide opportunities for young scientists, who are one of NIH's top priorities for support. The Core Center grants are designed to establish innovative programs of excellence by providing scientific and programmatic support for research by promising investigators. They provide funding to hire, provide appropriate start-up packages, and develop pilot research projects for newly independent investigators, with the goal of augmenting and expanding the institution's biomedical research base. We must invest today to ensure tomorrow's scientific discoveries.

ARRA Funds for Administrative Supplements

U.S. institutions and investigators with active NIH research grants may request administrative supplements for the purpose of accelerating the pace of scientific research through the programs and activities of their peer-reviewed projects. These supplements seek to promote job creation and retention, as well as scientific progress at NIH-funded institutions, by providing researchers with the means to employ, for example, postgraduate students or to enhance capacity for data analysis.

We are particularly delighted to tell you about our expanded summer program for teachers and students across America. Funds will provide short-term summer jobs for high school and undergraduate students—as well as elementary, middle, high school and community college science educators in laboratories around the country—work that will not only provide summer income, but will also provide several thousand young people with the opportunity to experience the world of research, and I hope will spark their desire to become scientists.

In addition to administrative supplements, U.S. research institutions and scientists with active NIH Research Grants may submit revision applications (so-called "competitive supplements") to support a significant expansion of the scope or research protocol of currently approved and funded projects.

The Economic Benefits

We are mindful that a top priority for the use of ARRA funds by NIH is to create and preserve jobs, as well as increase purchasing power in all corners of the country. We firmly believe that we can do this while carrying out the core NIH mission, and without compromising our commitment to fund the best scientific research ideas. In keeping with the ARRA reporting requirements, we are asking recipients to document key economic benefits, such as jobs created and retained. A study indicates that, on average, every NIH grant supports 6 to 7 in-part or full scientific jobs.[1] Another study suggests that every dollar spent by NIH in local communities around the Nation is leveraged on average three times its original amount, if you look at the national "economic multiplier" effect.[2] These grants pay the salaries of scientists and technicians. The scientists and technicians, in turn, purchase goods and services in the communities in which they work and live.

ARRA: Risk Management

NIH has implemented a risk management program in compliance with OMB guidelines that addresses the identification and assessment of proper controls over financial reporting and operations processes. In the financial arena, the risk program includes reviews of financial reporting at the transaction level that are conducted by both internal and external auditors. In the operations arena, the program includes internal assessments of systems and processes that support both intramural and extramural research.

The Scientific Benefits

The advancement of science is a gradual process. Groundbreaking discoveries are most often built on the foundation of many gradual advances that bring us closer to diagnosis, treatments, and other public health improvements expected by Congress and the American public. Because of ARRA funds, there may be many such discoveries across the country next year and many years thereafter. These discoveries could yield better understanding of the major diseases and disorders such as heart disease, cancer, neurodegenerative illnesses, autism, arthritis, mental health, chronic, acute and rare diseases, and diseases related to addiction or behavior.

We are committed to ensuring that ARRA funds will produce benefits to the economy, to scientific knowledge, and ultimately aid in improving the health of the Nation. As an agency, we are well-equipped to disburse these resources, to handle the increase in workload, and award grants expeditiously to the best scientists in the world.

Again, NIH is grateful for your trust and commitment to biomedical research and all the promise it brings to people here in the United States and around the world. We have employed a number of innovative strategies to quickly and wisely invest ARRA funds. We will provide you and the public with regular updates and reports to ensure full transparency and accountability for how these funds are being spent. Americans deserve to know the impact of their tax dollars—on science, on the economy, and the Nation's health. In addition, we look forward to working with you on the fiscal year 2010 budget request.

I would be pleased to answer any questions that you might have.

PREPARED STATEMENT OF JOHN E. NIEDERHUBER

Mr. Chairman and Members of the subcommittee: Thank you for the opportunity to offer testimony on behalf of the National Cancer Institute (NCI) and the National Cancer Program.

I am pleased to present the President's fiscal year 2010 budget request for the NCI of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $5,150,170,000, which is $181,197,000 more than the fiscal year 2009 appropriation of $4,968,973,000.

DOUBLING CANCER RESEARCH

The fiscal year 2010 budget reflects the President's prioritization of biomedical research supported by NIH. The budget is the first year of an 8-year strategy to dou-

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[1] "Estimating the Number of Senior/Key Personnel Engaged in NIH Supported Research," study issued October 2008. Study funded by the NIH Evaluation Set-Aside Program, 07–5002–OD–ORIS–OER, administered by the Evaluation Branch, Division of Evaluation and Systematic Assessment, OPASI, Office of the Director, National Institutes of Health.

[2] "In Your Own Backyard: How NIH Funding Helps Your State's Economy," published by Family USA (A Global Health Initiative Report). June 2008.

ble the NIH-wide cancer research budget and includes over $6 billion for this purpose. The budget balances the President's commitment to cancer research with that of research in other areas.

NIH's fiscal year 2010 budget will build upon the unprecedented $10 billion provided in the American Recovery and Reinvestment Act of 2009, which will support new NIH research on a wide array of diseases, condition, and disorders in 2009 and 2010.

Because cancer research involves the dissection and understanding of perhaps the most basic functions of human cell growth and differentiation, cancer research will always produce many serendipitous discoveries. Such discoveries involving the most basic properties of human cells have historically contributed to our understanding of the basic biology underlying almost all diseases.

In addition, cancer research also involves technology development that will benefit research in a number of disease areas. For example, cancer research includes a major effort to understand the complete genetic alterations that result in abnormal cell growth. This effort in whole genome sequencing is a major driver in the development of sequencing technology that we believe will lead to our ability in the next 2–3 years to perform whole genome sequencing in a matter of hours for less than $1,000.

Numerous other Institutes and Centers contribute their expertise to fundamental research on biological processes, technologies and tools, and work collaboratively with NCI to fund important research in cancer. For example, much of what has been learned at NCI in controlling tobacco usage is now being applied to study and address the growing health burden of obesity. NIH will work to ensure that cancer research resources are allocated responsibly, effectively, in accordance with peer review principles, and on the basis of sound science and cancer relevance.

MOVING PAST A LEGACY OF FEAR

One of the great American voices on behalf of biomedical research was Mary Lasker. A well-known figure in Washington politics and government, Mrs. Lasker was a driving force behind the creation of several Institutes of the NIH and a key player in the formulation and passage of the National Cancer Act of 1971. Among her towering accomplishments, however, one stands out, perhaps because of its simplicity. In the years after World War II, cancer, she once remarked, remained "a word you simply could not say out loud." Mary Lasker changed that. She persuaded David Sarnoff, the powerful head of the Radio Corporation of America—RCA—to allow the utterance on the airwaves of that single, chilling word.

Today, we feel no compulsion to avoid speaking its name; yet few would argue that we fear cancer less in 2009 than we did 50 or 100 years ago. Cancer will befall approximately 1 of 2 American men and 1 of 3 American women. Its diagnosis engenders thoughts of mortality, of debilitating treatments, of diminished quality of life, of lingering burdens on loved ones, of personal financial peril.

This major health problem is fueled by an aging, more heterogeneous population. A study published in April 2009 by the University of Texas M.D. Anderson Cancer Center estimated that the number of new cancer cases in the United States each year will increase by 45 percent over the next two decades, to 2.3 million per year by 2030.

It is thus quite understandable when the public and those responsible for health care ask if we are investing enough to advance the science needed to avert such predictions. Since 1971, the Federal Government, private foundations, and companies have spent approximately $200 billion on cancer research. This investment has led to our understanding of many of cancer's numerous complexities; has resulted in a steady decline in the annual overall cancer mortality—and has increased the number of cancer survivors to more than 12 million Americans. NCI's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism. Aggressive programs in screening and prevention have greatly reduced the incidence of a number of cancers. For example, NCI led efforts to eliminate the use of tobacco has resulted in a 1.9 percent decrease per year from 1992 to 2003 in male lung cancer incidence rates. This has accelerated to a 3.3 percent decline per year over the period from 2003 to 2006. Despite these advances, it is evident that a greater investment than ever is needed to continue the dissection of the fundamental biology underlying the initiation of abnormal cell growth and its progression to invasive and metastatic disease.

THE POWER OF THE GENOME

Cancer is an extremely complex disease of altered genes. These changes within the cells of our body take many forms—and are both inherited and acquired, as we

live out our lives. Since the completion of the Human Genome Project in 2003, the knowledge of the genetic alterations associated with cancer has grown exponentially. Vastly improved technologies are making it possible to study the genomes of thousands of individuals, in the search for common abnormalities that point to risk of cancer. Likewise, one of NCI's signature projects, The Cancer Genome Atlas (TCGA), is studying the genetic changes associated with the development of several cancer types, including lung, ovarian, and brain cancers. The success of this pilot program is leading NCI to expand TCGA's scope to the sequencing of 20 to 25 tumor types. Sequencing these tumors in more than 200 patients per tumor type, coupled with whole genome scans of large population cohorts, is uncovering important information about cancer risk and patient-specific profiles unique to disease. Within just 5 years, some have suggested, whole genome deep sequencing will be part of virtually every laboratory cancer experiment, and within a decade, such deep genomic sequencing will be commonplace for patients.

At this moment, the results of this deep probing of the genetic basis of cancer remain, in most cases, fascinatingly powerful information. How we turn that information—sometimes referred to as code—into new methods of prevention, early detection, and treatment of cancer will require a major infusion of new resources. We must convert this coded information, which is stored in large data sets, into a clear interpretation and understanding of the functional biological alterations these genetic changes impart. NCI is working to fill this large gap in our knowledge, through a well-considered, coordinated blueprint appropriate for a new era of medicine. It begins with new discoveries at the level of the gene and ends at the patient's bedside.

NCI is preparing to bring together a network of investigators, whose work will begin after genomic sequencing is completed, taking information generated by TCGA and allied projects and turning that data into new knowledge of biologic function. The goal will be to identify potential new therapeutic targets in molecular pathways and physical processes that are, today, considered "undruggable." This network will be virtual: a consortium of researchers primarily at research universities who will be offered the chance to participate in collaborative projects, often partnering between institutions. These projects will be prioritized on the basis of potential patient impact and technical feasibility—assigned to investigator sites on a competitive basis, each with a project manager.

The targets that will come forward from this functional biology consortium will be somewhat akin to a key piece of a jigsaw puzzle. It will be necessary to find the adjoining pieces—the new drugs, biologics, and other therapeutics—that connect. When potential new targets emerge, NCI will then employ its state-of-the art, high-throughput capacity to screen thousands of previously identified compounds, both natural and synthetic, to identify the exact piece to complete the puzzle.

In many cases, new therapies will require refinement, for example, to make them water soluble, or to create mass-producible versions of a natural product. Another virtual network, the Chemical Biology Consortium, will provide the necessary chemistry and chemists to optimize further development of these new anti-cancer agents. NCI will then be able to have those new agents produced in small batches for refinement and testing—using best manufacturing principles—and move them into preclinical testing, including toxicology screening.

Early phase clinical trials will follow. NCI has conducted the first of a new kind of trial called Phase 0, which uses a small number of carefully selected patients who, after receiving small doses of new drugs, are studied, in real time, at the molecular level, to see if the new medication is reaching and affecting its target. Phase 0 trials will allow for significantly earlier decisions on whether to move forward with Phase 1 trials.

It is not only Phase 0 trials that will require well characterized patients. As genomic characterization of the populace comes closer to becoming standard medical practice, NCI is taking steps on the leading edge of that transition, creating the first of a national network of patient characterization centers that will centrally conduct genomic and genetic characterization. Always employing the latest technologies and standardized protocols, these facilities will serve wide geographic areas, bringing together genomics and genetics, proteins and proteomics, all in the interest of matching a genetically characterized patient and his or her characterized tumor to appropriate and optimal therapeutic solutions.

The NIH Clinical Center; NCI's Specialized Programs of Research Excellence; the NCI Community Cancer Centers Program; Cooperative Groups; the Community Clinical Oncology Program; and the NCI-designated Cancer Centers network will all be key players in establishing a highly characterized national cohort of patients who can be easily matched with potential new agents.

DEVELOPING ELECTRONIC HEALTH RECORDS

Creating an integrated, 21st century translational science program will require data integration and a national commitment for the cancer electronic health record. NCI's cancer Biomedical Informatics Grid, better known as caBIGT, and its companion BIG Health Consortium, are leaders in this Federal effort, working to develop a unified biomedical information infrastructure, along with data standards and protocols for electronic medical records that are consistent with the Federal Government's national health IT efforts. Through caBIG, NCI is helping both large facilities from the NCI-designated Cancer Centers network and local facilities in the NCI Community Cancer Centers Program develop electronic records.

In addition, accomplishing the scale-up of TCGA and the genetic characterization of our patients—with data integration through caBIG—will require biospecimens collected using standardized protocols, tissue characterization, cataloging, and analysis, all coordinated by NCI's caHUB initiative.

A WIDE-RANGING EFFORT

This plan will require the contributions of biologists, chemists, informaticians, and clinical scientists devoted to a clear path from discovery to patient. This is not only the nature of translation; it will be a model for the study of many diseases and, ultimately, a model of 21st century healthcare. This platform is a vision for a new way of thinking. But it is not an unrealistic concept. It is an action plan: a roadmap for what we have begun to assemble this year, making the optimal use of every new resource.

In 2008, NCI began a series of meetings with theoretical physicists and mathematicians, designed to bring unique perspectives to the problem of cancer. The result is a new network of physical sciences—oncology centers, soon to launch, which will study physical forces—heat, stress, and cellular evolution, just to name a few—in cancer. This network is an exciting frontier in cancer research, which we fervently believe will be further proof that scientific collaboration pays great dividends.

NCI's goal is to make cancer a chronic condition one can live with, and not die from. We will continue to find better ways to prevent cancer's development and for the earliest detection, when a tumor is limited to a very small number of cells. We will continue to develop new therapies with fewer side-effects and greater quality of life. We will continue to study environmental causes of cancer. We will continue efforts to better understand the behaviors that increase cancer risk, and we will continue to follow those who have survived cancer, to understand the reasons why they are so often at risk for subsequent malignancies. These efforts will require coordinated programs and the continued work of a remarkable national cadre of individual laboratory investigators.

NCI is committed to paying dividends on behalf of every American. We no longer fear speaking the word cancer. Yet, our work is far from finished, and NCI remains committed to making every effort to advance a vastly different medical future.

Thank you for the opportunity to provide you this testimony. I look forward to the opportunity to take your questions.

PREPARED STATEMENT OF ELIZABETH G. NABEL

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). The fiscal year 2010 budget of $3,050,356,000 includes an increase of $34,667,000 over the fiscal year 2009 appropriated level of $3,015,689,000.

The NHLBI provides global leadership for a research and education program to promote prevention and treatment of heart, lung, and blood diseases. The vision is to enhance the health of all individuals and thereby enable them to lead longer and happier lives. The work of Institute is guided by the goals and approaches outlined in its strategic plan, which was completed and published in September 2007 and submits that its research projects re consistent with the President's multi-year commitment for cancer and autism.

This statement describes several initiatives that are being undertaken during the current fiscal year and outlines a number of opportunities to be addressed in fiscal year 2010.

STEM CELL CONSORTIUM

Recent advances in knowledge, coupled with development of new technologies and reagents, have set the stage for rapid progress in the field of regenerative biology

and medicine. The NHLBI is capitalizing on this extraordinary opportunity through formation of a Progenitor Stem Cell Biology Consortium that includes leading scientists in the fields of cardiovascular, pulmonary, and hematopoietic cell biology working closely with experts in the general field of progenitor cell biology. Its goal is to identify and characterize progenitor cell lineages, to direct the differentiation of stem and progenitor cells to desired cell fates, and to develop strategies to address the challenges presented by the transplantation of such cells. The Institute will fund 6 research hubs and 1 administrative coordinating center in fiscal year 2009, with plans for a total support period of 7 years.

CLINICAL TRIAL OF HYPERTENSION MANAGEMENT STRATEGIES

A new clinical trial, the Systolic Blood Pressure Intervention Trial (SPRINT), was launched in fiscal year 2009. The health benefits of lowering blood pressure in individuals with hypertension have been well demonstrated, and current practice strives to achieve a systolic blood pressure (SBP) level below 140 mmHg for most patients. However, epidemiological evidence suggests that the optimal SBP goal may be even lower. SPRINT will enroll about 7,500 individuals with hypertension or pre-hypertension, randomly assign them to a SBP goal of <120 mmHg or <140 mmHg, and assess cardiovascular disease outcomes. The potential public health impact of this work is substantial, given the multi-millions of people in this country and worldwide who suffer from high blood pressure.

ASTHMA NETWORK

The NHLBI has for many years supported highly successful clinical research networks designed to fill gaps in science and address emerging areas of concern in the management of asthma. Upon the anticipated end of the current funding period for the asthma networks, the Institute convened a workshop to obtain advice from key scientific leaders on a network structure that would sustain the past success and meet future clinical research needs. As a result of its recommendations, the Institute is establishing AsthmaNet, a clinical research network that will develop and conduct clinical trials of new treatment and management approaches in pediatric and adult populations. Launched in fiscal year 2009, AsthmaNet will include multiple clinical centers and one data coordinating center. The NHLBI's plans for promoting use of shared resources and promoting programmatic and scientific efficiency in the network coincide with the expansion of the NIH Roadmap initiative to Reengineer the Clinical Research Enterprise through the Clinical and Translational Science Award program.

HEMOGLOBINOPATHIES DATA SYSTEM

The NHLBI is developing and implementing a national data system and biospecimen repository on people with sickle cell disease, thalassemia, and hemoglobin E disease. It will be designed to collect, analyze, interpret, and disseminate State-specific data on the epidemiology, clinical characteristics, healthcare utilization, and community resources of patients with these conditions. The system will support research, information dissemination, policy decisions, healthcare planning, and provider training at the social, State, and national levels. This fiscal year 2009 initiative is being conducted via an interagency agreement with the CDC.

CARDIAC TRANSLATIONAL RESEARCH IMPLEMENTATION PROGRAM (C–TRIP)

A new program has been designed to accelerate the movement of laboratory discoveries to the bedside of patients with heart failure or arrhythmias. C–TRIP is a two-stage project to speed translation of promising new therapeutic interventions derived from basic research through well-designed clinical trials to demonstrate safety and efficacy. Two-year stage 1 exploratory planning grants, to be awarded in fiscal year 2010, will support feasibility studies, analysis of existing data, preparation for regulatory clearances, team-building, development of clinical management tools and recruitment strategies, and finalization of protocols. Subsequently, stage 2 grant applications will be considered for the conduct of the safety and efficacy trials.

NEW PROGRAMS TO PREVENT AND TREAT CHILDHOOD OBESITY

Obesity is a major cause of morbidity and mortality, and effective interventions are urgently needed to address this increasingly prevalent public health menace. A new research consortium will test the efficacy of innovative approaches to prevent weight gain among normal-weight young children and to prevent additional weight gain or facilitate weight loss among obese adolescents.

A second fiscal year 2010 initiative will examine outcomes associated with existing community programs designed to reduce childhood obesity by improving children's diet and physical activity. One research unit will be funded to serve as a study coordinating center, which will work with the National Collaborative on Childhood Obesity Research to design and implement the research. The study will establish common metrics for evaluation of the programs and examine outcomes associated with program policies, environments, educational activities, dietary and physical activity regimens, and other factors. The goal is to inform national and local policy for control of childhood obesity.

RESUSCITATION OUTCOMES CONSORTIUM (ROC) RENEWAL

In 2004 the NHLBI, the American Heart Association, the U.S. Department of Defense, and several Canadian health agencies established the ROC to design and conduct studies of promising experimental strategies to resuscitate patients who experience out-of-hospital cardiac arrest or life-threatening trauma. The ROC brings together investigators, hospitals, emergency medical services (EMS), and local communities to address the unique characteristics of this research and ensure the efficient translation of proven strategies into clinical practice. In addition to supporting new trial protocols, the 2010 renewal will develop information to define and improve prehospital best practices, facilitate public health efforts for the prevention of emergency life-threatening conditions, and improve EMS delivery and training.

PREMATURITY AND RESPIRATORY OUTCOMES PROGRAM (PROP)

The new PROP will promote collaborative, innovative research to identify mechanisms, and associated biomarkers of respiratory disease risk of premature infants who are ready for discharge from the neonatal intensive care unit. Increased survival of very premature infants is leading to increasing numbers of children with chronic lung disease that often results in multiple readmissions. Currently no objective measures exist that can be used to predict which premature newborns will have persistent respiratory problems after discharge from the hospital. This cooperative, multidisciplinary scientific group will investigate hypotheses on the molecular mechanisms that make certain premature newborns prone to develop recurrent respiratory disease, with the long-term goal of improving outcomes in the first year of life.

NHLBI PROTEOMICS INITIATIVE

The Institute will continue to invest substantial resources in the use of proteomic approaches and technologies to develop a greater understanding of pathway and interactions that influence heart, lung, and blood diseases. Planned for fiscal year 2010 is a combined renewal of the NHLBI Proteomic Centers and the NHLBI Clinical Proteomic Program, both of which terminate in September 2009. Each of seven centers will focus on proteomic technology development and molecular mechanistic and functional studies related to a specific clinical need, problem, or disease. The ultimate goal of this work is to bring greater precision, reliability, and sensitivity to detection, diagnosis, treatment, and prevention strategies for the individual patient.

We are delighted to have the opportunity to pursue these exciting new research avenues. I would be pleased to answer any questions the subcommittee may have.

PREPARED STATEMENT OF ANTHONY S. FAUCI

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Allergy and Infectious Diseases (NIAID), of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $4,760,295,000, which is $57,723,000 more than the fiscal year 2009 appropriation of $4,702,572,000.

NIAID conducts and supports biomedical research to understand, treat, and prevent infectious and immune-mediated diseases of domestic and global concern, including HIV/AIDS, tuberculosis, malaria, neglected tropical diseases, emerging and re-emerging infectious diseases. NIAID's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism. As economies and societies around the world have become increasingly interdependent, responding to emerging infectious diseases, such as the 2009-H1N1 influenza virus, as well as to long-established health challenges such as neglected tropical diseases, has taken on new urgency. As we address infectious diseases in a global context, we have the added benefit of contributing to preparedness against

the threat of bioterrorism and naturally occurring disease outbreaks. Meanwhile, our ongoing research on domestic health challenges such as HIV/AIDS, influenza, and asthma, allergies, and other immune-mediated diseases continues to yield important advances. Using a multidisciplinary approach that engages academic, industry, governmental, and nongovernmental partners, NIAID remains committed both to basic immunology and infectious disease research and the application of this knowledge to the development of strategies to detect, prevent, and treat these diseases.

The research activities of NIAID will become more important than ever, as current and as-yet unrecognized health threats, particularly in the context of the inevitability of emerging and re-emerging infectious diseases, will require new diagnostic, preventive, and therapeutic interventions. These new tools promise to have a great impact on the public health over the next two decades.

We have long known that the threats posed by infectious microbes do not remain static, but change over time as new microbes emerge and familiar ones re-emerge with new properties or in new settings. This will not change in the coming decades. Addressing these global threats requires that we consider infectious diseases not through the lens of individual diseases, infections, or microbes in a vacuum, but by understanding how diseases interact in people with multiple health issues. Only then can we develop the tools for a comprehensive and practical approach to global health.

Tuberculosis (TB) is a prototypic example of a re-emerging threat as an increase in the prevalence of drug-resistant forms of TB presents major challenges to the control of this disease. TB also is an example of a disease that often occurs with other infectious diseases such as HIV/AIDS—people co-infected with TB and HIV appear to have a more rapid and deadly disease course. Recently, NIAID-supported clinical trials have shown that mortality among TB patients co-infected with HIV is remarkably reduced when antiretroviral (ARV) therapy is provided at the same time as TB therapy. Additional studies are under way to determine optimal strategies for the prevention, treatment, and diagnosis of TB in the setting of HIV infection. NIAID continues to conduct and support research to create a foundation of knowledge for the discovery of new diagnostics, drugs and vaccines for TB, including drug-resistant TB. The Institute's support for public-private partnerships has been instrumental in linking research across sectors to build a robust pipeline of tools to combat TB.

Malaria continues to exact a devastating toll on individuals worldwide, mostly among children in sub-Saharan Africa. Compounding the problem is the emergence of drug-resistant malaria parasites and insecticide-resistant mosquito vectors. In 2008, the Institute released the NIAID Strategic Plan for Malaria Research and the NIAID Research Agenda for Malaria. The Plan and Agenda outline our efforts to accelerate control and move toward eradication of malaria through biomedical research, including the development of prevention modalities, promising drugs and vaccine candidates. Accomplishing these goals will require the support and cooperation of malaria researchers and other organizations to build on the foundation of NIAID's basic research program in malaria. Over the next two decades, we hope to have a major impact on global TB and malaria burden through the development of vaccines that protect against these infectious killers.

Seasonal influenza, which changes slightly every year, is the classic example of a re-emerging infectious disease. Influenza viruses also can undergo more drastic genetic changes that periodically enable them to evade pre-existing immunity and cause a pandemic, such as the deadly influenza pandemic in 1918 that killed more than 50 million people worldwide. NIAID has seen significant progress in its influenza research program, particularly in the area of pandemic influenza preparedness. This progress has prepared the Institute to respond rapidly to the newly identified 2009-H1N1 influenza virus, which has emerged as a public health threat in the United States, Mexico, and throughout the world. NIAID-funded researchers have responded quickly to this new threat, characterizing the virus and preparing for the development of a vaccine and other countermeasures.

Nearly 28 years since the first cases of AIDS were documented, the terrible burden of HIV/AIDS continues to grow. The 2.7 million new infections worldwide in 2007 underscore the continuing urgency of the global AIDS pandemic, and sobering HIV/AIDS statistics in the District of Columbia remind us that the AIDS epidemic here in the United States demands our strongest efforts. Over the past two decades, NIH and NIAID—supported by Congress and by this subcommittee—have devoted substantial resources to the fight against HIV/AIDS.

Worldwide, for every two people who receive ARV treatment, five others are newly infected. Therefore, our first priority in the fight against HIV/AIDS is prevention. NIAID-supported investigators have made great strides in advancing our under-

standing of the modalities of effective prevention, including those that prevent mother-to-child transmission of HIV. NIAID-supported research recently determined that medically supervised circumcision of adult males markedly reduces the risk of HIV acquisition through heterosexual intercourse for at least 3.5 years after the procedure, demonstrating long-term efficacy of male circumcision as a prevention tool. Research conducted by our Microbicide Trials Network found the microbicide gel PRO 2000 to be safe and showed the first suggestion of potential efficacy among several clinical trials with other products. Of course, the most powerful prevention tool would be a safe and effective HIV vaccine. In response to the significant challenges that United States and international vaccine investigators have experienced in HIV vaccine development, NIAID has expanded our basic vaccine discovery research portfolio to provide the knowledge necessary to identify a viable HIV vaccine candidate. Our hope is that these advances in HIV prevention research will become part of a comprehensive HIV prevention "toolkit" that will markedly decrease new infections over the next two decades.

In addition to these prevention modalities, NIAID is boldly advancing three new approaches to HIV prevention. Together with Government and nongovernmental partners, the Institute is investigating the feasibility of pre-exposure prophylaxis (PrEP) for HIV prevention, which involves providing ARVs to HIV-negative individuals who are at high risk of HIV infection. Second, recent modeling data have shown that aggressive HIV testing and treatment potentially could reduce the number of new HIV cases by 95 percent in the next decade; NIAID is evaluating critical research questions that underpin the validity of this voluntary "test and treat" approach. Finally, NIAID is expanding its efforts to find a cure for HIV/AIDS. Through research to improve our basic understanding of HIV viral latency, we hope to achieve long-term HIV remission following discontinuation of effective therapy—a "functional" cure—or, ultimately, a complete eradication of residual virus.

Since the acceleration of our biodefense research program in fiscal year 2003, NIAID has achieved major successes in the development of countermeasures against significant bioterrorism threats. Some countermeasures have been fully developed and are stockpiled or available for use in an emergency; others in the pipeline have been transferred to the HHS Biomedical Advanced Research and Development Authority for advanced development. Promising candidate countermeasures in development include ST–246, a smallpox drug candidate that has protected animals from an otherwise lethal exposure to live poxviruses.

Equally important, NIAID has developed a physical and intellectual research infrastructure that has been critical to our ability to respond to new and re-emerging infectious diseases. This year, the Institute recompeted the Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases, which comprise a network of 11 regionally based, multi-institutional centers engaged in interdisciplinary research to develop vaccines, therapeutics, adjuvants and diagnostics for biodefense and emerging infectious diseases.

Autoimmune diseases, allergic diseases, asthma, rejection of transplanted organs, and other immune-mediated disorders are significant causes of chronic disease and disability in the United States and throughout the world. NIAID-supported research in immunology and immune-mediated diseases has led to significant advances in our understanding of the mechanisms underlying these diseases and in the development of strategies to detect, prevent, and treat them.

For example, food allergies affect the health and quality of life of many Americans, particularly young children. NIAID remains committed to basic research and clinical studies to advance the understanding of food allergy and food allergy-associated anaphylaxis. In June 2008, NIAID awarded twelve 2-year grants, totaling $2.5 million, to investigators to lead high-impact, innovative studies of food allergy under the Exploratory Investigations in Food Allergy initiative. Cosponsored with the Food Allergy and Anaphylaxis Network, the Food Allergy Project, and the U.S. Environmental Protection Agency, this program supports innovative pilot studies on the mechanisms of food allergy, with a goal of attracting new investigators to the field of food allergy research. We plan to renew this program in fiscal year 2010.

NIAID also continues to support clinical trials to prevent the development of food allergies and to reverse established allergy to milk, eggs, and peanuts. Lastly, NIAID, in collaboration with professional societies, advocacy groups, and other Federal agencies, is developing clinical guidelines to provide guidance to medical practitioners on the diagnosis, management, and treatment of food allergies.

For more than six decades, NIAID has conducted and supported basic research on infectious and immune-mediated diseases that has underpinned the development of vaccines, therapeutics, and diagnostics. These, in turn, have improved health and saved millions of lives in the United States and around the world. Through partnerships with academic, industry, governmental, and nongovernmental partners, the

Institute will continue to leverage these fundamental discoveries into the tools needed to achieve a healthy world.

PREPARED STATEMENT OF DR. ROGER I. GLASS, DIRECTOR, FOGARTY INTERNATIONAL CENTER

Mr. Chairman and members of the subcommittee: I am pleased to present the President's budget for the Fogarty International Center (FIC) of the National Institutes of Health (NIH). The fiscal year 2010 budget of $69,227,000 includes an increase of $536,000 more than the fiscal year 2009 appropriated level of $68,691,000.

Over the past year, Congress has renewed its commitment to confronting global health issues, recognizing that these investments will not only improve the health and well-being of all, but also enhance U.S. stature abroad, economic development, and U.S. competitiveness. As the recent H1N1 virus outbreak illustrates, solving health problems in an interconnected world requires greater international collaboration than ever before. To effectively confront complex health issues that transcend national boundaries, scientific collaborations must be continually developed and nurtured. Research advances are more likely to occur when investigators study diseases on-site, and U.S. scientists partner with international scientists to develop health interventions that are responsive to local and international needs and priorities. This model requires a critical mass of trained, in-country scientists and capable institutions that are uniquely positioned to address local study populations and to support sustainable collaborations with U.S. and other investigators.

Since its inception, the Fogarty International Center (FIC) has been the focal point for global health at the NIH. FIC supports and facilitates global health research conducted by U.S. and foreign investigators, builds collaborations between U.S. and health research institutions worldwide, and trains the next generation of scientists to address global health needs. FIC-supported research and research training programs address a wide range of diseases and needs, including HIV/AIDS, malaria, Tuberculosis and other infectious diseases; noncommunicable diseases, such as brain disorders and cancer; and cross-cutting areas that foster sustainable research environments, including research ethics and informatics for health research. In 2008, FIC launched a strategic plan that addresses emerging areas of science and shifting disease burdens, and strengthens the global health research workforce in the United States and around the world.

ADDRESSING THE RISING BURDEN OF NONCOMMUNICABLE DISEASE

Rapidly developing countries like India, Brazil, Mexico, China, and Bangladesh have seen life expectancies grow for the past 40 years. Population forecasts now predict that by 2030, 1 out of 8 people will be 65 or more than 1 billion adults. In addition, poorly balanced nutrition, less physical activity, and tobacco use are all on the rise in developing countries as a result of poverty, industrialization, urbanization and global marketing of goods and products. With increasing longevity, convergence of risk factors and diseases blurs the distinction between disease burdens in developing and developed countries, and calls for a common health research agenda. International research collaborations to study these diseases in highly endemic areas accelerate scientific advances on how to prevent and treat them. In response to this trend, FIC established the new Millennium Promise Awards in Non-Communicable Disease Program in partnership with several other NIH Institutes, designed to support research training in low- and middle-income countries in fields related to cancer, stroke, lung diseases, obesity, and environmental factors.

According to the World Health Organization, tobacco use kills 5.4 million people every year—an average of 1 person every 6 seconds. Almost half the world's children breathe air polluted by 8 causes of death in the world. If current smoking patterns continue, this number will rise to 8 million in 2030, with approximately 80 percent of the deaths occurring in developing countries. FIC, in partnership with the National Cancer Institute and the National Institute on Drug Abuse, is helping to address this rising epidemic through its International Tobacco and Health Research and Capacity Building Program. This program enhances the ability of scientists in low- and middle-income nations to understand risk factors for smoking uptake, particularly in youth, to develop effective prevention and mitigation programs, and to identify the most effective implementation and communications strategies to reduce the negative impacts of smoking on populations. The knowledge gained and effective interventions developed abroad through the Tobacco Program will also benefit U.S. populations who share common risk factors with low-resource communities in developing countries.

The continuing burden of infectious disease in low-income populations, as well as the rapid rate at which microbial agents can evolve, adapt and develop resistance to antibiotics, demand that FIC continue to invest in infectious disease research and training. In particular, FIC will continue to support interdisciplinary research that develops predictive models and principles governing the transmission dynamics of infectious disease agents. This will result in increased capacity to forecast outbreaks and improved understanding of how diseases like the H1N1 flu emerge and re-emerge, and strategies to control them.

ADVANCING IMPLEMENTATION SCIENCE

Unprecedented resources are being invested in interventions that have been proven safe and effective, although many have not been implemented on a wide scale due to logistical, cultural, financial, and other barriers. Bridging the gap between effective interventions and improved health outcomes will in large part depend on a cadre of local scientists who can ask and answer questions regarding what works, what does not, and why, in particular settings. To advance this area of science FIC supports research training for scientists who can generate knowledge to improve scale-up of interventions and help identify the most effective ways to translate research findings into clinical and public health practice.

For example, FIC's International Clinical, Operational, and Health Services AIDS/TB Research Training Program is developing a network of researchers who are studying how to best apply research knowledge and new technologies related to HIV/AIDS and TB in clinical and community settings. With support from this program, scientists in Haiti have developed a new masters degree in public health program at a Haitian university and are training the personnel needed to monitor and evaluate the implementation of a new country-wide program to provide a standardized package of HIV care and prevention to 300,000 people per year.

MAINTAINING U.S. LEADERSHIP IN GLOBAL HEALTH RESEARCH

If we are to continue to lead in biomedical research, then U.S. researchers must be supported to effectively participate in international science. Biomedical research has always been an inherently international enterprise. Many significant scientific advances have resulted from research conducted by teams of scientists working across international borders. For example, U.S. and local scientists together pioneered the development of oral rehydration therapy (ORT) for treatment of cholera. ORT is now the first line treatment for childhood dehydration worldwide and recommended for treatment of every American child with diarrhea. In this era of globalization, this trend will not only continue, but will likely become stronger. It will also require a well-trained cadre of U.S. health scientists who are able to work seamlessly in diverse settings.

To this end, FIC support strengthens the ability of U.S. academic institutions to engage in the global scientific marketplace. The vast majority of FIC awards support scientists in U.S. institutions, who in turn collaborate with colleagues in foreign institutions. Additionally, FIC is capitalizing on the burgeoning interest in global health on U.S. university campuses through two innovative programs. First, we are providing a launching pad for American health sciences students and junior researchers to build relationships abroad and to address critical global health research questions through the Fogarty International Clinical Research Scholars Program (FICRS). This program responds to the acute need for future clinical investigators who can help translate basic research advances into clinical practice on a global scale. This next generation of clinical researchers will require hands-on experience in conducting clinical trials and clinical research in countries where the disease burdens are highest. The FICRS provides highly motivated U.S. graduate students in the health sciences and medical residents or fellows 1 year of mentored clinical research training at distinguished low- and middle-income country research institutions. Each U.S. student is paired with a foreign student, who also receives training as an equal partner, thus strengthening scientific capacity in the United States and abroad simultaneously. Several NIH Institutes partner with FIC in the effort, and therefore, the program includes a wide breadth of research areas, including cancer, maternal and child health, and extensively drug-resistant TB.

An increasing number of U.S. and foreign academic research institutions are welcoming the opportunity to use their substantial creative resources to make a significant and lasting difference in global health. As scientific problems become more complex, there is a need for team and systems approaches to tackle important health challenges. To help catalyze this approach in academic research institutions, Fogarty's Framework Programs for Global Health support the development of multidisciplinary global health programs on campuses in the United States and in low-

and middle-income countries. This innovative program develops new curricula and degree programs that cut across departments and schools to create a pipeline for a new generation of researchers schooled in multiple fields to address global health challenges. Schools representing more than 17 different disciplines participate in the program including, engineering, environmental sciences, journalism, business, law, medicine and public health.

Congressman Fogarty was prescient in arguing that the needs and rewards of global health research will benefit the United States as well as the global community. FIC is extending his vision, given that international trade, travel and communications have created a truly interdependent world. As we look to the next two decades, we envision a world in which a global scientific workforce is equipped with the knowledge and the skills to better prevent and treat disease as a result of rigorous global research. This workforce will form the backbone of research institutions in the United States and abroad, which will be effectively linked with each other through years of sustained productive research and training collaborations. Working towards this vision moves us closer to the ideal of global health—one that reflects the aspiration of all people to live long and healthy lives.

PREPARED STATEMENT OF DR. JOSEPHINE P. BRIGGS, DIRECTOR, NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $127,241,000, which is $1,770,000 more than the comparable fiscal year 2009 appropriation of $125,471,000.

In December 2008, the NCCAM, in conjunction with the National Center for Health Statistics, released data from the 2007 National Health Interview Survey (NHIS).[1] The survey is the most comprehensive and reliable information to date on the use of complementary and alternative medicine (CAM) in the United States. The 2007 NHIS data confirm that millions of Americans—38 percent of U.S. adults and 1 in 9 children—use CAM to promote health and wellness and to address specific conditions such as chronic pain.

The NHIS data affirm the public health importance of NCCAM's mission to develop an evidence base for the integration of CAM with conventional healthcare and to disseminate research results to the public and healthcare professionals. Since its founding 10 years ago, NCCAM has created a nationwide CAM research enterprise, built on sound scientific principles, that enables the rigorous study of CAM. Among NCCAM's accomplishments are a Centers of Excellence program at leading biomedical research institutions; standards for quality and stability for the natural products used in research; and the development of tools and methodologies to discover the potential benefits and risks of CAM modalities. Today, under NCCAM's leadership, partnerships between biomedical research institutions and CAM institutions and practitioners are engaged in state-of-the-art scientific research. NCCAM-supported CAM research has resulted in more than 3,300 peer-reviewed publications. Professional associations, such as the American College of Physicians and the American Academy of Orthopedic Surgeons are now able to use CAM research findings to inform their practice guidelines. NCCAM will continue to meet the challenges of building the evidence base for CAM interventions through its rigorous research, research training, and outreach endeavors. NCCAM's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism.

A STRUCTURED APPROACH TO ANSWERING KEY QUESTIONS

CAM research is a promising scientific endeavor that requires multidisciplinary basic, translational, and clinical trial collaborations. In fiscal year 2010, NCCAM will fund awards under a new initiative, Partnerships for Complementary and Alternative Medicine Clinical Translational Research. This initiative, which replaces the NCCAM Developmental Centers for Research on CAM program, will foster such collaborations at CAM institutions and create tools and methodologies for research.

NCCAM investigations span the continuum of research areas: basic (How does the therapy affect the body?); translational (Do we have the methods and tools to detect and measure the modality's effects?); efficacy (Is there evidence of safety and benefit

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[1] Barnes PM, Bloom B, Nahin R. CDC National Health Statistics Report#12. Complementary and Alternative Medicine Use Among Adults and Children: United States, 2007. December 10, 2008.

under optimal research conditions?); and effectiveness (How well does the CAM practice work in the "real world" and in comparison to other treatments?). NCCAM has strong programs in all four of these areas; its current research strategy places particular emphasis on strengthening effectiveness research.

AREA OF PROMISE AND INVESTMENT: MANAGING CHRONIC PAIN

The 2007 NHIS data indicate that chronic pain is, by far, the most common health problem for which Americans turn to CAM. NCCAM-supported basic, translational, and clinical research is using state-of-the-art neuroscience, brain imaging, and novel study designs to demonstrate that mind-body medicine approaches, such as massage, chiropractic, and acupuncture, affect pain perception and to understand how patient expectancy and practitioner reassurance may have an impact on pain management. For example, using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), basic researchers are developing important insights into how acupuncture affects specific pain networks in the brain. In addition, emerging data, such as the recent report in the Annals of Internal Medicine that massage therapy and simple touch may provide pain relief for advanced cancer patients, point to the promise of mind-body practices. NCCAM is focusing on developing the evidence base for the use of nonpharmacologic CAM practices for pain management.

Chronic back pain is a problem for millions of Americans, and costs associated with it total at least $50 billion annually.[2] It is often difficult to treat, and medications used to address it can have troubling side effects. Certain CAM therapies, such as acupuncture, chiropractic, massage, and yoga, show promise in treating chronic back pain. In May 2009, NCCAM is sponsoring, with other NIH Institutes and Centers, a workshop on nonpharmacologic interventions for the treatment of chronic back pain, bringing together experts to identify gaps in the CAM evidence base and opportunities for future research. NCCAM plans to fund awards in fiscal year 2010 under a new initiative, Effectiveness Research—CAM Interventions and Chronic Back Pain. This initiative will support studies of CAM approaches to address a range of outcomes for back pain, such as reduced dependency on narcotics.

AREA OF PROMISE AND INVESTMENT: TRANSLATIONAL TOOLS

Basic and translational (i.e., "bench-to-bedside") research is especially challenging for CAM mind-body practices, acupuncture, and body-based and manipulative therapies, because current scientific methods may not adequately capture and measure the effects of these therapies. To decipher these practices' potential physiological effects and enable scientists to study them in clinical trials, better scientific tools, metrics, and methodologies must be developed. In fiscal year 2010, NCCAM will fund awards under its initiative, Program for Translational Tools for CAM Clinical Research. The research supported under this initiative will improve the quality and reproducibility of CAM clinical investigations.

AREA OF PROMISE AND INVESTMENT: NATURAL PRODUCTS

According to the 2007 NHIS, almost 40 million U.S. adults and 2.850 million children use natural products to manage their health and wellness. Given the widespread use of dietary supplements, NCCAM's research into the safety and efficacy of natural products remains a public health priority.

NCCAM-supported studies, including collaborations under the NIH Botanical Research Centers program, demonstrate the promise of natural products research. For natural products, basic and translational research remains critical precursors to large-scale clinical trials. A recent study by the University of Maryland and Rutgers University elucidated an immune system mechanism of action of green tea polyphenols on rheumatoid arthritis. In another study, Duke University researchers reported that bromelain, an enzyme derived from pineapple stems, reduced inflammation resulting from Crohn's disease and ulcerative colitis.

Although natural products research shows great promise, product quality remains a significant issue. In July 2008, an NCCAM-funded study in the Journal of the American Medical Association reported that one-fifth of Internet-available Ayurvedic medicines contained detectable levels of lead, mercury, and arsenic. The authors also found evidence for benefit of industry-established standards for quality in reducing levels of toxic metals. NCCAM has led the scientific community in requiring that all natural products used in its research undergo quality and stability screen-

[2] Low Back Pain Fact Sheet; National Institute of Neurological Disorders and Stroke, National Institutes of Health, Department of Health and Human Services, July 2003.

ing to ensure that the research is safe and reproducible. Ongoing collaborations with the dietary supplement industry are important to this effort. Equally important are NIH partnerships in the development of an evidence base for natural products.

MAKING WISE DECISIONS: OUTREACH

Studies confirm that consumers do not tell their doctors that they use CAM, and doctors do not ask their patients about CAM use. To ensure safe, coordinated care NCCAM developed its time to talk patient and provider education program. NCCAM also partnered with the National Institute on Aging to develop a CAM section on NIH Senior Health, the NIH Web site especially for older adults.

In fiscal year 2009, NCCAM will initiate a new educational section of its Web site (nccam.nih.gov) to provide health professionals with evidence-based information and clinical practice guidelines on CAM use. NCCAM also cosponsored the North American Research Conference on Complementary and Integrative Medicine, on May 12–15, 2009. This international meeting of scientists and CAM and conventional practitioners highlighted the emerging science on CAM and future directions for research.

NCCAM: LOOKING TO THE FUTURE

There are areas of considerable promise and potential for the field of CAM research, and NCCAM will focus its resources to ensure that they will be optimally directed. The Center has begun to develop its next strategic plan, seeking the input of the scientific community as well as its diverse community of stakeholders. As a first step in this process, the Center has convened a Blue Ribbon Panel to consider future directions for its intramural research program.

Thank you for the opportunity to testify. I would be pleased to answer the subcommittee's questions.

PREPARED STATEMENT OF DR. BARBARA M. ALVING, DIRECTOR, NATIONAL CENTER FOR RESEARCH RESOURCES

Mr. Chairman and members of the subcommittee: It is a privilege to present to you the President's budget request for the National Center for Research Resources (NCRR) for fiscal year 2010. The fiscal year 2010 budget of $1,252,044,000 includes an increase of $25,781,000 more than the fiscal year 2009 appropriated level of $1,226,263,000. NCRR's funding priorities for fiscal year 2010 include expansion of the Clinical and Translational Science Awards (CTSA) program. Additionally, NCRR will sustain the range of activities supported by the Center's other major programs, including the Research Centers in Minority Institutions, the Institutional Development Awards, the National Primate Research Centers, and the Biomedical Technology Research Centers.

The mission of the NCRR, as one of the 27 Institutes and Centers of the National Institutes of Health (NIH), is to provide support and training for researchers that extend from the laboratory to clinical trials and into dissemination of prevention strategies and treatments that will impact communities as well as patients.

APPRECIATION FOR INVESTMENT IN RESEARCH INFRASTRUCTURE

On behalf of NCRR and the research community, I extend our appreciation to the President and the Congress for the $1.6 billion allocated to our Center as American Recovery and Reinvestment Act (ARRA) funding. We will ensure that the $1 billion for extramural construction funding and the $300 million in shared instrumentation funds are invested wisely at academic institutions throughout the Nation. The NCRR is using the additional ARRA funding to supplement awards in the Institutional Development Award (IDeA) program, the Research Centers in Minority Institutions (RCMI) program, the Clinical and Translational Science Award (CTSA) program, as well as other NCRR programs.

BUILDING A MATRIX FOR CLINICAL AND TRANSLATIONAL RESEARCH

The NCRR, through its stewardship of the IDeA, RCMI, and CTSA programs, is linking investigators and communities by supporting and encouraging collaborations for training, sharing of data, accelerating advances in research and clinical informatics, and dissemination of best practices for community engagement. For example, the University of Washington CTSA is partnering with academic institutions in IDeA States to create greater opportunities to reach underserved populations. CTSAs are also connecting with RCMIs: Emory University (Atlanta) is partnering with Morehouse School of Medicine; Vanderbilt University (Nashville, Tennessee is

partnering with Meharry Medical College; and Weill Cornell Medical College (New York) is partnering with Hunter College.

Led by NCRR, the CTSA program is a partnership between the NIH and a national consortium of 39 academic health centers and research institutions to build academic homes for clinical and translational research. The CTSA program is designed to translate more efficiently the rapidly evolving knowledge developed in basic biomedical research into treatments to improve human health. Additionally, the CTSAs are training a new generation of clinical and translational researchers to excel in the interdisciplinary, team science environment.

The momentum of the national CTSA consortium continues to build as new connections are rapidly emerging within, across, and beyond the consortium. In the last year, 15 new CTSAs joined the consortium, adding representation from 5 new States, additional pediatric expertise, and greater informatics capabilities. When the program is fully implemented, the NCRR expects to fund CTSA awards at 60 institutions at a total cost of $500 million per year. As the CTSA program increases in complexity and size, institutions are forming regional consortia to focus on shared goals with greater efficiency.

The CTSA institutions are using business principles and practices to improve the processes involved in translational research. Investigators and core facilities directors at the CTSA at Yale University are increasing efficiencies and reducing redundancies by using Web-based resources and systems to maximize the use of their core research facilities, which include imaging, informatics, and genomic. Thanks to this integration, researchers now have improved access to sophisticated technologies and valuable expertise with less administrative burden.

The CTSA consortium has identified five strategic goals: (1) to develop strategies and resources to move laboratory discoveries into early clinical testing (T1 translation); (2) to reduce complexities and improve ways clinical and translational research is conducted; (3) to enhance training and career development of clinical and translational investigators; (4) to encourage consortium-wide collaborations; and (5) to improve the health of communities across the Nation.

FOSTERING T1 TRANSLATIONAL RESEARCH

The potential to accelerate research discoveries from the bench into early clinical studies (T1) usually requires preclinical studies, those studies that involve the appropriate animal models. Currently, researchers with expertise in animal models (including mouse, rat, and nonhuman primate models) are working with CTSA investigators on pilot projects that focus on cardiovascular disease, ovarian cancer, and other diseases. NCRR and its National Primate Research Centers are working closely with National Institute of Allergies and Infectious Diseases and the NIH Office of AIDS Research to ensure that adequate numbers of animals and resources are available to meet the need for development of new AIDS vaccines.

NCRR's Biomedical Technology Research Centers are cutting-edge interdisciplinary centers that create transformative technological and computational infrastructure for biomedical research. The CTSAs are leveraging the expertise of investigators in these centers to conduct a wide range of translational research, from cell biology to clinical imaging.

LEVERAGING PARTNERSHIPS TO BENEFIT BIOMEDICAL SCIENCE

The CTSAs are realizing returns on their research discoveries by securing patents and licensing them. From 2006 to 2008, the CTSAs established more than 350 academic, public, and private partnerships. To achieve its overall mission to speed the translation of scientific discoveries to improve human health, the CTSAs are establishing innovative partnerships with industry to accelerate the development of treatments, diagnostics, and devices. For example, the CTSA at Scripps Research Institute is collaborating with Qualcomm to develop and clinically validate biosensors—tiny devices that measure body functions—and other wireless healthcare technologies. Similarly, the Oregon Health and Science University is partnering with Intel to apply wireless and mobile technology with various sensors to enable earlier detection and treatment of life-threatening events for diabetics and individuals at high risk of stroke.

Ensuring that the public is actively engaged in research and benefiting from research findings is a key component of the CTSA program. One example of ways CTSAs are improving the health of their communities is a collaborative effort in Houston, which is helping children in two inner-city neighborhoods make healthier lifestyle choices and reduce their risk of obesity. CTSAs in Chicago have joined forces to ensure active participation from their communities throughout all stages of research—from project design to results dissemination. Similarly, connections be-

tween the CTSA consortium and NCRR's Science Education Partnership Award program are growing, helping to inspire the next generation of researchers. As an example, the University of Pittsburgh CTSA and Science Education Partnership Award investigators hosted an outreach event for middle school students, featuring a mobile science laboratory.

IMPROVING RESEARCH INFORMATICS

NCRR continues to support informatics tools and resources to enhance research collaboration. For example, NCRR is funding a Biomedical Informatics Research Network coordinating center at the University of Southern California to enhance data sharing among the network's research centers and other researchers. Through an ARRA-funded initiative, NCRR will facilitate interdisciplinary collaboration and scientific exchange by developing tools and infrastructure that will help connect basic, clinical, and translational investigators and students with other researchers that share their interests or who could benefit from their expertise. NCRR also plans to support development of an animal models informatics resource to provide researchers with one-stop access to information related to animal models of human disease.

EXPANDING RESEARCH CAPACITY

NCRR is enhancing the capabilities of RCMIs to conduct clinical and translational science through the RCMI Infrastructure for Clinical and Translational Research Awards. Funding may be used for out-patient clinical resources, biostatistical support, core laboratories, and patient-oriented research infrastructure. This award is a reorganization of previous RCMI programmatic activities and will enhance research capacity, improve collaboration between translational and clinical researchers, facilitate multidisciplinary training and career development and enable seamless interactions with CTSAs.

The IDeA program fosters health-related research and increases the competitiveness of investigators in 23 States and Puerto Rico. NCRR's previous investments in developing research capacity through its IDeA program have resulted in additional funding opportunities for investigators. For example, the University of Kansas recently received $9.6 million in grants from non-Federal sources for drug development efforts; the expertise that provided the foundation for this award grew, in part, from funding for a center of excellence in the IDeA program.

This snapshot of NCRR's programs and activities demonstrates our continuing commitment to advancing clinical and translational research. NCRR's budget request and its research projects are consistent with the President's multi-year commitment to finding cures for cancer and autism. By encouraging collaboration among our clinical and translational programs, NCRR is maximizing the Nation's investment to translate research discoveries into improved treatments for patients.

PREPARED STATEMENT OF DR. PAUL A. SIEVING, DIRECTOR, NATIONAL EYE INSTITUTE

Mr. Chairman and members of the subcommittee: I am pleased to present the President's budget request for the National Eye Institute (NEI). The fiscal year 2010 budget of $695,789,000 includes an increase of $7,309,000 more than the fiscal year 2009 appropriation level of $688,480,000.

OPHTHALMIC GENETICS

The loss of sight affects us in fundamental ways, threatening independence, mobility, and quality of life. Many eye diseases strike later in life. Thus, as life expectancy has increased, more Americans have become susceptible to vision loss and blindness. One such disease, age-related macular degeneration (AMD), is the leading cause of vision loss in the United States. AMD causes a progressive loss of light-sensing cells in the macula, the center of the retina, making it difficult to read, recognize faces, drive a car, or perform even simple tasks that require hand-eye coordination. Based on published study data, 8 million older Americans are at risk to develop advanced AMD.

Advanced AMD can take two distinct forms, either geographic atrophy or wet AMD. In geographic atrophy, large areas of the retina atrophy and die. In wet AMD, abnormal blood vessels grow into the retina, leaking blood and serum that damages the retina. Previous studies have found several gene variants, which regulate inflammation, are associated with the "wet" type of AMD. These variants are thought to lead to chronic, overactive inflammatory responses that damage retinal tissue and eventually lead to AMD. Most recently, the first gene associated exclusively with the

geographic atrophy, namely the Toll-like receptor 3 (TLR3) gene, was published. The TLR3 gene encodes a viral sensor which activates immune responses. When TLR3 activates in response to certain viruses, it induces cell death in the retina thus causing geographic atrophy. Alternatively, in humans, it appears that low activity of TLR3 confers protection against geographic atrophy, most likely by sparing the death of retinal cells. This is the first evidence that viral infection may contribute to the development of geographic atrophy. Ongoing work includes screening for viruses in affected individuals as well as developing methods to decrease TLR3 activity in the retina.

Glaucoma is a group of eye disorders that share a distinct type of optic nerve damage, which can lead to blindness. Elevated intraocular pressure is frequently, but not always, associated with glaucoma. Published study data find that approximately 2.2 million Americans have glaucoma and a similar number are unaware that they have developed the disease. Like AMD, glaucoma is a genetically complex disease likely involving many changes in many genes. NEI is committed to exploiting the latest genetic technologies in finding the genes that contribute to this common disorder. To this end, NEI initiated funding for genome-wide association studies, a powerful approach that enables investigators to scan the entire human genome to detect multiple, subtle gene variants that increase the risk of developing this complex, blinding disease. Knowledge of the genetic basis of glaucoma is crucial to developing personalized therapies that target specific genes in order to prevent vision loss.

Each genetic discovery has made it possible to study the implicated gene's function in health and disease. NEI investigators have made considerable progress in understanding the molecular mechanisms of genetic eye disorders and are developing rational therapies that address the molecular cause of the disease. The first success in this translational research effort are the reports of positive results from recent phase I clinical trials of gene transfer in a form of Leber congenital amaurosis, a severe, early onset retinal disease. In the effort to accelerate progress NEI established eyeGENE, a research program that offers genetic testing to patients through a national network of vision research laboratories in exchange for participation in a secure, confidential patient registry and DNA repository. DNA samples and corresponding diagnostic and clinical information are made available to the vision research community to recruit patients for clinical trials and to conduct genetic and molecular studies. eyeGENE represents a new paradigm to personalize medical care in the practice of ophthalmology. Knowledge of an individual's genomic profile will enable patients to make informed decisions about presymptomatic, preventive treatments or highly targeted molecular therapeutics.

TRANSLATIONAL MEDICINE

Neovascularization refers to the growth of new blood vessels. In some diseases, such as diabetic retinopathy and AMD, neovascularization is mistakenly activated and becomes a major pathologic consequence of the disease. Neovascularization can cause severe and irreversible vision loss due to abnormal vessel growth and consequent fluid leakage into the retina. Previous studies have established vascular endothelial growth factor (VEGF) spurs neovascularization and several therapies have been developed to prevent the abnormal activation of the VEGF protein. A recent National Institutes of Health (NIH) supported study reports on the discovery of a protein, Roundabout4 (Robo4), that stabilizes the existing vasculature and prevents neovascularization by inhibiting VEGF activity. Robo4 maintains vascular integrity by inhibiting VEGF-induced cell migration, vessel formation, and permeability. Vascular eye diseases are the most common cause of vision loss in the United States. This study suggests a new and promising therapeutic avenue to control neovascularization by regulating Robo4 activity.

RNA interference is a new approach that has been touted as having great potential for treating many diseases. This method harnesses a naturally occurring process that cells employ to control gene expression. By designing a small, interfering RNA sequence (siRNA), it is thought investigators can target and silence specific genes with specific siRNAs. Vision researchers have developed siRNA sequences to prevent the expression of VEGF in AMD and diabetic retinopathy that have been demonstrated to prevent neovascularization in animal models. However, a recent NEI-supported study suggests that siRNA may not always target the intended gene to initiate RNA interference. This study provides an important cautionary note to the entire field of siRNA that systemic administration of this treatment may have unintended consequences and side effects.

VISUAL NEUROSCIENCE

Although the function of astrocytes, a cell type found in the brain and central nervous system, is not entirely understood, they have long been thought to maintain normal neuronal function. More recent evidence suggests that astrocytes may have some function in neural signaling and processing. Recently, NEI investigators found key evidence that astrocytes also act as a critical intermediary between neurons and local blood flow. In this study, inhibition of astrocyte activity decreased local blood flow. This finding explains why imaging devices, like functional MRI, detect blood flow changes that correspond to neuronal activity. Pathologic changes in astrocytes are implicated in Parkinson's, Alzheimer's, and other neurodegenerative diseases. The specific effect of astrocyte activity on the hemodynamic response provides a basis for the interpretation of functional MRI, adding qualitatively to the clinical and research utility of this powerful imaging tool across the broad spectrum of neurologic disease.

CLINICAL TRIALS AND DIAGNOSTICS

Cataracts (clouding of the ocular lens) remain the primary cause of blindness in the world today. Researchers at NEI and NASA collaborated to develop a dynamic light scattering device which allows clinicians to detect and quantify the amount of unbound alpha crystallin proteins in an intact eye. With this device, it is now possible to safely and reproducibly measure the extent of lens damage and cataract formation caused by oxidative stress to a patient's eye (and perhaps the body) by measuring alpha crystallin reserves. This provides clinicians with the ability to monitor lens health, and may allow preventive or therapeutic actions that delay or eliminate cataract formation and blindness.

Each year approximately 33,000 Americans undergo corneal transplants to replace diseased corneas, the normally transparent tissue that protects the eye and helps focus light on the retina. Corneal transplants are among the most common and successful transplantation procedures in medicine but sufficient donor is not available. Eye banks, the primary source of donor tissue, refrain from harvesting tissue from donors over age 65 because of uncertainty about the integrity of older corneas. However, the recently published Cornea Donor Study (CDS) found that corneal transplants using tissue from older donors, ages 66 to 75, have similar success rates as tissue from younger donors, ages 12 to 65. Based on these findings, the study authors recommend that the age limit for donor tissue should be expanded to 75. The CDS study gives eye banks, transplant surgeons, and patients confidence in the use of older donor tissue. This finding should help eye banks keep pace with the demand for corneal tissue.

MEDICINE OF THE FUTURE

Development of an artificial cornea will provide an abundant source of nonimmunogenic tissue for transplantation. Cell transplantation has prevented vision loss in rodent models of retinal disease. It is likely that these efforts will culminate in viable forms of regenerative medicine for eye disease. Genomic medicine will allow us to predict susceptibility to disease and pre-empt it with a variety of gene-based therapies. Gene transfer will likely become an option to treat many retinal degenerative diseases. We will have the opportunity to restore ambulatory vision to the blind through new prosthetic devices that reproduce vision electronically. Such devices will allow those with untreatable conditions to maintain independence and mobility. While there is much work ahead, current research efforts to treat and cure eye disease are very promising.

CANCER RESEARCH PORTFOLIO

NEI funds basic research on cell biology, development and the regulation of blood vessel growth where findings could have relevance to our understanding and treatment of cancer. NEI also supports a phase III clinical trial on the treatment of retinoblastoma, a cancerous, blinding and potentially fatal eye disease. Consistent with the fiscal year 2010 NIH priority to expand cancer research funding, NEI will increase its fiscal year 2010 commitment to this portion of the portfolio by 4.4 percent.

PREPARED STATEMENT OF DR. ALAN E. GUTTMACHER, ACTING DIRECTOR, NATIONAL HUMAN GENOME RESEARCH INSTITUTE

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Human Genome Research Institute (NHGRI) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $509,594,000, which is $7,227,000 more than the fiscal year 2009 appropriation of $502,367,000.

NHGRI's budget request and its research projects are consistent with the President's multi-year commitment for cancer.

WINDFALL OF DISCOVERIES OF THE GENETIC BASIS OF DISEASE

The Nation's previous investments in the Human Genome Project and the International HapMap Project have moved research forward into many diseases with unprecedented speed. HapMap-enabled genome-wide association studies (GWAS) identify a stunning number—more than 130 in 2008 alone—of genetic factors associated with major causes of morbidity and mortality in the United States, such as autism, diabetes, cardiovascular disease, lung and prostate cancer, and inflammatory bowel disease. Identification of gene variants associated with disease raises the possibility of using genetic testing, in combination with family history information, to identify susceptible, pre-symptomatic subjects for screening and preventive therapies. It also provides key new understanding of the gene-environment interactions and biological pathways that lead to disease, thus providing new insights into treatment and prevention.

THE CANCER GENOME ATLAS

Initiated in fiscal year 2007, the TCGA is a pilot project, jointly supported and led by the NHGRI and the National Cancer Institute (NCI) that applies a comprehensive, large-scale genomic analysis approach to cancer research. TCGA is designed to develop and test the complex scientific and technological approaches needed to identify the mutations and other genomic changes associated with various types of cancer. Three NHGRI-supported sequencing centers provide genomic sequencing capability for the TCGA. In fiscal year 2008, the first major results of this pilot project were obtained for the most common form of brain cancer, glioblastoma multiforme. Another very exciting result was an unexpected observation that points to a potential mechanism of resistance to a common chemotherapy drug used for brain cancer. These first results from the TCGA pilot project represent an exciting indication of the value of the multi-dimensional analysis of the molecular characteristics in human cancer. In the next 1 to 2 years, the focus of TCGA will be on two other common cancers, squamous cell lung cancer and ovarian cancer, as well as further analysis of glioblastoma (brain cancer), as well as potential scale up to deal with many other forms of cancer.

MEDICAL SEQUENCING

The NHGRI's medical sequencing program aims to drive continued technology improvement (lowering the cost of genome sequencing) and to produce data useful to biomedical research. Seven studies are currently underway to identify the genes responsible for several relatively rare, "single-gene" diseases and to survey the range of gene variants that contribute to certain common diseases. In fiscal year 2008, a number of medical sequencing projects were initiated: (1) Sequencing the genomic regions identified in genome-wide association studies as containing genetic components underlying common diseases, such as diabetes, breast cancer, schizophrenia, or Crohn's disease; (2) Sequencing the genomes of important human pathogens, such as those that cause malaria and sleeping sickness, and their invertebrate vectors (in collaboration with the National Institute of Allergy and Infectious Disease; and (3) the TCGA project.

PERSONALIZED GENOMIC MEDICINE

In addition to basic research underway to support medical applications of genomics, two clinical genomics initiatives launched in fiscal year 2007 are now in full stride. The first, ClinSeq, is a pilot study aimed at developing technological and procedural approaches to facilitate large-scale medical sequencing in a clinical research setting. The second, the Multiplex Initiative, is a study intended to provide genetic susceptibility testing for several common health conditions, such as cardiovascular disease and osteoporosis, to evaluate patients' reactions to the testing and receipt of results.

THE 1000 GENOMES PROJECT

The 1000 Genomes Project builds on the human haplotype map developed by the International HapMap Project to produce a much more comprehensive view of genomic variation. In fact, it aims to find almost all the variants in the genome, including those that contribute to disease risk. The 1000 Genomes Project will map not only the single-letter differences in people's DNA, called single nucleotide polymorphisms, but also will produce a high-resolution map of larger differences in genome structure called structural variants, which are rearrangements, insertions, deletions, or duplications of DNA segments. The importance of these structural variants has become increasingly clear from surveys completed in the past 18 months that demonstrate that differences in genome structure may play a role in susceptibility to such conditions as mental retardation and autism.

The project includes large-scale implementation of several new sequencing platforms to capitalize on the cost reductions emerging from evolving technologies, described in the journal Nature Biotechnology in October 2008. Using standard DNA sequencing strategies, the effort would likely cost more than $500 million. However, the cost of the project is expected to be far lower to the program—$30 million to $50 million—due to the project's pioneering implementation of new technologies.

LARGE-SCALE SEQUENCING

Currently, 197 genomes are either in the pipeline or have been completed by the NHGRI-supported large-scale sequencing centers, which are world leaders, renowned for their cost-effective and high-quality work. Completed in fiscal year 2009, the most recent study of a cow was an important development in agriculture that may lead to higher-quality beef and milk production and possibly lower carbon dioxide emissions. Ongoing sequencing targets include several nonhuman primates, mammals, fungi, and multiple strains of yeast.

THE $1,000 GENOME

The NHGRI's continuing commitment to the development of innovative sequencing technologies, which reduces the cost and increases the speed of DNA sequencing, fuels the swift pace of genomic discoveries. In the past year, several groups have demonstrated the ability to work with individual DNA strands and read individual DNA bases. These two breakthroughs are being combined to deliver the ability to sequence DNA isolated directly from cells without any processing apart from purification. This is one technology with promise to achieve the goal of sequencing a genome for $1,000 by 2014, NHGRI's original goal.

GENOMIC FUNCTION

The NHGRI supports research to identify and characterize the function of all parts of our genome and to understand their biological relevance. Efforts to uncover functional elements are not limited to the human genome, since understanding the genomes of other, "model," organisms also can give insight into the structure and function of the human genome.

Following a successful pilot project, the NHGRI implemented a full-scale ENCyclopedia of DNA Elements (ENCODE) Project in fiscal year 2007 to examine the entire human genome for sequence-based functional elements. Concurrently, the NHGRI initiated modENCODE, which has similar goals for the analysis of the genomes of two important model organisms. This program will take advantage of the small, more manageable genomes of these organisms to unlock the function of the many genes they share with humans.

ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS

The NHGRI supports six Centers of Excellence in Ethical, Legal, and Social Implications (ELSI) Research. The Centers focus on issues surrounding large-scale genomics research and emerging genetic technologies. The NHGRI continues to support ELSI research as a core aspect of our research portfolio in an effort to anticipate and address the societal issues that will continue to arise as we learn ever more about the human genome and its contributions to human health and disease.

MOVING FORWARD

The NHGRI recently began two new programs to harness genomic knowledge and technology to help patients whose needs are not met by existing scientific and medical programs. Launched in 2008, the Undiagnosed Diseases Program (UDP), jointly led by the NHGRI, the NIH Clinical Center, and the Office of Rare Diseases Re-

search, focuses on the most puzzling medical cases referred to the NIH by physicians across the Nation. The NIH Therapeutics for Rare and Neglected Diseases (TRND) Program, launched in fiscal year 2009, builds upon the technology and strategies of high-throughput genomics to identify and shepherd novel therapeutics for diseases where the risks of failure are currently too high for the private sector, but the human need is too great to ignore. These conditions by definition either occur in fewer than 200,000 Americans or in the developing world, limiting the profit motive for industry. UDP and TRND exemplify how the country can leverage the advances funded and developed by the NHGRI and the NIH to drive the development of more personalized, predictive, pre-emptive, and participatory diagnostic and therapeutic options, improving health outcomes for all Americans.

PREPARED STATEMENT OF DR. RICHARD J. HODES, DIRECTOR, NATIONAL INSTITUTE ON AGING

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute on Aging (NIA) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $1,093,143,000, which is $12,347,000 more than the fiscal year 2009 appropriation of $1,080,796,000.

Our Nation is currently in the midst of an unprecedented demographic shift. The number of Americans ages 65 and older is expected to double within 25 years. In less than 50 years, the number of "oldest old"—people ages 85 and older—will more than quadruple. As record numbers of Americans reach retirement age and beyond, profound changes will occur in our economic, healthcare, and social systems.

The NIA leads a national effort to understand the nature of aging and the diseases and conditions that are more common among older adults and to develop interventions that will help older adults enjoy robust health and independence, remain physically active, and continue to make positive contributions to their families and communities. We support and conduct a comprehensive and integrated portfolio of genetic, biological, clinical, behavioral, and social research related to the aging process, healthy aging, and diseases and conditions that often increase with age.

UNDERSTANDING HEALTHY AGING AND DISEASE AND DISABILITY

Modern medicine and new insights into lifestyle and other environmental influences are allowing a growing number of people to remain healthy and socially and emotionally vital into advanced ages, and NIA remains at the forefront of the Nation's efforts to identify the genetic, physical, emotional, and environmental factors that contribute to healthy old age. For example, researchers on the NIA-supported Long Life Family Study are analyzing data from families with two or more siblings over age 79 to identify factors that may contribute to long and healthy life, and the Longevity Consortium brings together leading researchers to facilitate the discovery, confirmation, and understanding of genetic determinants of longevity. NIA intramural investigators are continuing the SardiNIA Project to search for genes associated with nearly 100 traits in a small, genetically homogeneous population and the Age, Gene/Environment Susceptibility (AGES) Study to explore genetic susceptibility and gene/environment interactions that contribute to various health outcomes in old age.

NIA's biology programs are wide ranging and address organs, systems, and processes throughout the body. For example, the Institute supports research on long-term weight maintenance, diet composition, and energy balance as well as the role of nutrition in the prevention of common age-related conditions such as heart disease and cancer. NIA is also collaborating with the National Institute of Allergy and Infectious Diseases to support research to better understand the mechanisms underlying age-related decline of the thymus, an organ that produces white blood cells known as T cells, a critical component of the body's ability to launch a robust immune response against infections. Studies on basic bone biology have led to the surprising finding that the protein Lrp5, an important factor in the process through which new bone is created, regulates bone mass formation through serotonin synthesis in the intestine, and not by acting directly on the bone, as was previously believed. This finding broadens our understanding of bone remodeling and suggests new therapeutic approaches to increase bone mass. Research initiatives to help us better understand mechanisms of anemia, chronic kidney disease, and thyroid dysfunction in the elderly have also been established at NIA, and an advisory "summit" meeting was held in September 2008 to identify areas of scientific opportunity and facilitate the formulation of future plans for research on the underlying biology of aging-related changes.

Cognitive aging is a high-priority research area for NIA. A new focus on brain health, as opposed to the study of specific causes of brain disease and dysfunction, has emerged in recent years and has become an increasingly important paradigm in neuroscience research. NIA is continuing its involvement with the trans-NIH Cognitive and Emotional Health Project to coordinate and accelerate research leading to interventions for neurological health, as well as with the NIH Neuroscience Blueprint Toolbox initiative on the development of assessment tools for cognitive and behavioral health. NIA also continues to support studies of age-related changes in cognition, including grants funded under two new and related research initiatives—one to develop neural and behavioral profiles of normal cognitive aging and one to develop interventions to remediate age-related cognitive decline as distinct from Alzheimer's disease (AD) or related conditions.

PROMOTING HEALTHY AGING AND PREVENTING AGE-RELATED DISEASE AND DISABILITY

NIA is continuing to support the development of interventions to maintain health and prevent age-related disease and disability. For example, NIA-supported researchers are conducting a number of studies aimed at reducing the incidence and severity of falls, the leading cause of both fatal and nonfatal injury among older adults in the United States. Ongoing studies are exploring the association between vitamin D insufficiency and fall risk; examining the effects of neighborhood environmental characteristics on risk of outdoor falls; and focusing on development of strategies to improve strength, balance, and gait in the elderly.

The NIA-supported Advanced Cognitive Training for Independent and Vital Elderly Study was the first randomized, controlled trial to demonstrate long-lasting, positive effects of brief cognitive training to forestall cognitive decline in older adults. However, the training did not improve the participants' ability to tackle everyday tasks. More research is needed to translate the findings from the laboratory into interventions that are effective at home. In 2008, NIA solicited research to convert insights from previous work in cognitive aging into feasible intervention strategies, including cognitive training, lifestyle interventions, dietary interventions, or behavioral change that can be tested in randomized clinical trials. Investigators are encouraged to develop interventions addressing the role of individual differences in cognition, personality, and sociocultural factors in mediating or moderating adherence and outcomes. This research will be active in 2010.

The development of interventions that will extend life span as well as health span is another emerging area of study. Through the innovative Interventions Testing Program, NIA-supported researchers are investigating promising treatments, including diets, pharmaceuticals, and nutritional supplements, that have the potential to extend the life span and delay disease and dysfunction in mice, with the long-term goal of identifying those interventions most likely to have a beneficial effect in humans. Fourteen compounds are currently under study, with 3 more slated to be added in 2009. Testing on these compounds will continue through 2010.

EARLY DETECTION, DIAGNOSIS, AND TREATMENT OF AGE-RELATED DISEASE

Improved technologies as well as advances in our understanding of the mechanisms of disease are allowing for the development of interventions to predict, detect, diagnose, and treat age-related disease and disability. Scientists in NIA's groundbreaking Alzheimer's Disease Neuroimaging Initiative have made a significant step forward in developing a test to diagnose the early stages of AD earlier and more accurately by measuring two biomarkers—tau and beta-amyloid proteins—in cerebrospinal fluid. The investigators found that certain changes in biomarker levels in cerebrospinal fluid may signal the onset of AD. They also established a method and standard for testing of these biomarkers.

NIA currently supports more than 30 clinical trials of interventions to prevent, slow, or treat AD. Interventions under study include a highly promising immune approach; hormonal treatments, including testosterone and raloxifene; diabetes drugs such as metformin and insulin; antioxidants; physical and mental exercise; commonly used psychiatric drugs; and many others. The identification of imaging and biological markers as well as the development of improved clinical and neuropsychological evaluation methods will enable us to perform less expensive, shorter, and more efficient intervention trials.

In addition, NIA supports studies of treatments for a variety of other conditions including new therapies for menopausal hot flashes; hormone supplementation in men with symptoms related to low levels of testosterone; and cognitive behavioral therapy for older adults with arthritis pain and insomnia. A follow-up study to the ground-breaking Diabetes Prevention Program established the efficacy of a lifestyle intervention and drug treatment that can sharply decrease the risk of type 2 diabe-

tes in overweight individuals, which was most pronounced for individuals age 60 or over.

ADDRESSING THE SOCIETAL IMPLICATIONS OF AN AGING POPULATION

The social and economic implications of aging are multi-faceted. NIA supports long-term studies of older Americans covering a wide range of topics, including retirement and economic status, care giving, behavioral medicine, the dynamics of health and functional change at older ages, cognition, and long-term care. These studies include the ongoing Health and Retirement Study, the leading source of combined data on health and financial circumstances of Americans over age 50 and a valuable resource to follow and predict trends and help inform health policy. NIA also supports studies on the social, emotional, cognitive, and motivational processes and neurobiological mechanisms of economic behavior as these influence social, financial, and health-related decisions of middle-aged and older adults.

One of NIA's most urgent priorities is to improve our ability to reduce health disparities and eliminate health inequities among older adults. NIA works to identify ways to reduce health disparities through its Resource Centers for Minority Aging Research, and the Institute has compiled a Web-based toolkit on outreach, recruitment, and retention of minority populations in clinical research on aging. Through the Healthy Aging in Neighborhoods of Diversity Across the Life Span Study, NIA intramural researchers are continuing their efforts to disentangle the complex relationships among race, socioeconomic status, and health outcomes. Other programs, notably the NIA Alzheimer's Disease Centers, have a strong focus on minority health and health disparities in both research and outreach.

Once again, thank you. I welcome your questions.

PREPARED STATEMENT OF DR. KENNETH R. WARREN, DIRECTOR, NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute on Alcohol Abuse and Alcoholism (NIAAA), of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $455,149,000, which is $4,919,000 more than the fiscal year 2009 appropriation of $450,230,000.

NIAAA's long-range vision for medicine with respect to alcohol-related health issues is that research on the health effects of alcohol will reduce the burden of illness attributable to excessive alcohol consumption thereby enhancing the well-being of individuals at risk, their families, and society-at-large. Through translation of NIAAA supported research findings, we have an unparalleled opportunity to significantly reduce the burden of illness due to alcohol-related problems. We are especially appreciative of the American Recovery and Reinvestment Act funds which will accelerate our progress. NIAAA's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism.

CURRENT SCOPE OF THE PROBLEM AND RESEARCH

According to the Centers for Disease Control and Prevention, alcohol is the third leading cause of preventable death in the United States. Even more important from a public health perspective, alcohol misuse negatively affects the quality of life for millions of Americans. According to the World Health Organization, alcohol is one of the top 10 causes of Disability Adjusted Life Years in the United States and contributes to a number of the other leading causes. Alcohol problems cost the United States an estimated $185 billion annually, with almost half the cost resulting from lost productivity due to alcohol-related disabilities.[1] According to NIAAA's National Epidemiological Survey on Alcohol and Related Conditions, more than 18 million people ages 18 and older suffer from alcohol abuse or dependence and only 7 percent of them receive any form of treatment. Furthermore, heavy drinkers, who are not dependent, but nevertheless at risk for adverse health and psychosocial outcomes, are seldom identified. The consequences of alcohol misuse can affect both drinkers and those around them at all stages of life, from damage due to alcohol exposure of the developing embryo, to injuries, to tissue and organ damage resulting from chronic, heavy alcohol use. Therefore, to achieve its goal of reducing the heavy burden of illness from alcohol misuse, NIAAA's research focus must be broader than

[1] Harwood, H. Updating Estimates of the Economic Costs of Alcohol Abuse in the United States: Estimates, Update Methods and Data (2000).

simply reducing alcohol-related mortality; it must encompass reducing the risk for all adverse alcohol-related outcomes at all stages of life.

Research supported by NIAAA has reframed our understanding of alcohol dependence in several ways by demonstrating that: (1) it is a developmental disorder that often has its roots in childhood and adolescence; (2) the highest prevalence of alcohol dependence in the U.S. general population occurs in 18–24 year olds; (3) there is substantial variation in the severity and chronicity of dependence among individuals; and (4) a large percentage of individuals with alcohol dependence are highly functional in society, and therefore go largely unnoticed by the healthcare system.

These findings underscore the opportunity to: (1) be able to better predict which individuals are at risk for future dependence by understanding the complex interplay between genetic, environmental, and developmental factors; (2) pre-empt future problems through research-based prevention efforts for children and adolescents as well as screening and guidance for people of all ages about how drinking patterns, especially binge drinking, relate to adverse health outcomes; (3) conduct research to develop treatment options that are personalized to individual needs and lifestyles; and (4) engage individuals, communities, and professional groups to be actively participatory in shaping the future of healthcare as it relates to alcohol misuse.

OUTLOOK FOR THE FUTURE

NIAAA is revolutionizing alcohol treatment by providing evidence-based options for addressing the full range of alcohol- related problems. For example, research has shown the value of alcohol screening in primary care and mental health settings to help patients understand the risks associated with different drinking patterns. NIAAA has developed tools that clinicians can use to screen and intervene in these settings. Moving treatment of less severe forms of alcohol dependence into mainstream medical care will decrease stigma, improve availability, accessibility, and appeal of treatment options, and ultimately reduce the number of people who suffer with dependence. Alcohol-dependent patients will benefit from NIAAA's research focusing on the development of new treatments including behavioral therapies and medications that will shorten the duration, number, and severity of episodes of dependence and prevent, for most, the development of chronic, relapsing dependence. Studies suggest that as a result of these types of intervention, most people with mild to moderate dependence will recover.

Patients with more severe and/or relapsing dependence, are more complex to treat and often need multi-faceted, personalized addiction services that may include medications, counseling, psychotherapy, and case management. These patients often have other health (infectious diseases, mental illness, and liver disease) and psychosocial (family, marital, and workplace) problems, some that are the direct result of their alcohol misuse. Comprehensive treatment must take all of these into account. NIAAA-supported research will continue to develop and refine treatment options for these individuals, both for their alcohol dependence as well as the many adverse health consequences that may result. Collectively, these changes in the approach to treatment of alcohol problems will substantially reduce the public health burden of heavy drinking and alcohol use disorders.

Ensuring that appropriate research-based guidance about alcohol use for special populations, including pregnant women, is available and will result in a dramatic reduction in the incidence of fetal alcohol spectrum disorders, the most severe forms of which produce lifelong disability, and may also decrease the incidence of Sudden Infant Death Syndrome. NIAAA research will continue to inform this guidance, including information about the risks of alcohol exposure to the developing embryo and fetus, and will make it accessible to primary healthcare providers and obstetricians. For pregnant women who drink despite the best advice, research is focused on developing nutritional and/or pharmacological agents that may lessen the negative effects of alcohol exposure.

Biomarkers, stemming from NIAAA-supported genetic and epigenetic research, will be available that: (1) predict individual risk for future alcohol dependence; (2) assess progression of at risk drinking through dependence; and (3) track damage to tissue and organs. These tools will enhance the ability of healthcare providers to offer guidance to patients about their drinking patterns and determine appropriate healthcare based on individual risk factors. A repertoire of medications will facilitate treatment tailored to the needs of the patient. Personalized treatment including medications and behavioral therapies will be based on individual genetic make-up, desired drinking outcomes, attention to co-occurring disorders, ease of compliance, and other factors.

MOVING FORWARD

NIAAA supported biomedical and behavioral research is supporting the research that will contribute to realizing the vision outlined above. Ongoing studies, as well as new initiatives, will provide the scientific knowledge and tools, to improve our ability to predict which individuals are at increased risk for alcohol-related problems including dependence, pre-empt the harm from alcohol misuse, and provide personalized treatment.

The integration of routine alcohol screening, and where appropriate, brief intervention and/or referral to specialty treatment into primary healthcare for all ages is central to reducing consequences of alcohol misuse. NIAAA will continue to develop teaching and training tools to increase the usage of A Clinician's Guide: Helping Patients Who Drink Too Much. NIAAA has also recently launched Rethinking Drinking, a new Web site, and booklet that provides information and tools to help individuals change harmful drinking patterns, either on their own or by helping them reach the decision to seek help. NIAAA is also developing guidance on screening and brief intervention for children and adolescents, recognizing that criteria developed for adults may not fit the needs or behaviors of youth.

Medications development remains a central focus of the Institute. Emerging data are changing the way we look at alcohol dependence, guiding us to be more strategic about the medications we test, the way we test and design them, and how we determine the subpopulations of patients most likely to benefit from them. For example, new understanding of the relationship between withdrawal induced anxiety and relapse has provided additional targets for drug development to minimize relapse. Broadening the desired treatment outcome, from targeting only abstinence to including reduction in heavy drinking, is also influencing the medications that are being tested as well as how they are tested. Other compounds that may mitigate tissue and organ damage are under study.

Most individuals with alcohol dependence do not access treatment yet many of them recover without the benefit of professional care or facilitated self-help. NIAAA continues to investigate the process leading to a decision to stop drinking or to seek help. In concert with a broader NIH Roadmap Initiative, NIAAA is currently supporting studies to understand mechanisms of change away from harmful health behaviors.

Given our current state of knowledge and what we are learning from ongoing studies, we are optimistic that we can substantially reduce the burden of illness for alcohol-related problems and the suffering it brings to individuals, their families and society at large.

PREPARED STATEMENT OF DR. STEPHEN I. KATZ, DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget for the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $530,825,000, which is $5,953,000 more than the fiscal year 2009 appropriation of $524,872,000.

INTRODUCTION

As the primary Federal agency for supporting medical research on diseases of the bones, joints, muscles, and skin, the NIAMS touches the lives of nearly every American. For example, the U.S. Bone and Joint Decade notes that 1 in 2 people will experience back pain each year, and 1 in 5 will have pain that affects their ability to work. The National Arthritis Data Working Group estimates that 21 percent of adults have arthritis in at least one joint, a figure that is likely to grow as the population ages. Likewise, 1 of every 2 women and 1 in 4 men aged 50 years and older suffer fractures each year because of osteoporosis; researchers project that the number of osteoporotic fractures in the United States will grow from 2 million to more than 3 million in the next two decades. The NIAMS is committed to preventing disabilities and reducing costs associated with these and other conditions through balanced basic, translational, and clinical research investments.

As the Institute sets priorities, it is considering how recent advances have positioned its research community for discoveries to prevent disease and improve each American's life. It is soliciting input from researchers, healthcare providers, patients, and the public on promising areas of inquiry; pressing scientific needs; programs to ensure a continuing supply of well-trained researchers; and strategies to eliminate health disparities. An important consideration is how investigators can

engage in multidisciplinary opportunities. Chronic pain, for example, is an aspect of many diseases that are part of the NIAMS portfolio; staff are exploring partnerships through the Trans-NIH Pain Consortium. Prospects for stem cell research are growing rapidly as researchers isolate stem cells from skin and other organs, and as more lines become available under the Nation's policy for Federal support of embryonic stem cell research.

Consistent with the Federal commitment to double NIH-wide cancer research spending, the NIAMS will continue to pursue collaborations with the National Cancer Institute in support of high-quality projects that relate directly to diseases and organ systems within the NIAMS mission, particularly the bones and the skin. Already, the NIAMS supports research on mechanisms underlying skin cancers, and investigators have uncovered a strategy that kills tumor cells with less damage to healthy skin.

PREVENTIVE MEDICINE

Research to identify susceptibilities to and initial symptoms of disease, and to develop strategies to slow disease progression, is a NIAMS priority. Building on findings that early, aggressive therapy alters the course of rheumatoid arthritis (RA), NIAMS is comparing treatments against a related disease-juvenile idiopathic arthritis.

The NIAMS and the National Institute on Aging lead the Osteoarthritis Initiative (OAI), a public-private partnership to identify and evaluate biomarkers of osteoarthritis (OA). NIH and its partners, with input from the Food and Drug Administration, launched the OAI in 2001. More than 1,100 researchers worldwide have accessed OAI data to explore issues such as differences in OA progression, or why only some people with X-ray evidence of OA develop pain. In 2010, the NIH will extend the OAI for 6 years. It expects the OAI to suggest approaches for slowing joint damage, facilitate clinical testing of interventions and allow clinicians to identify risk factors for OA development, predict severity, and personalize treatments for their patients.

COMPLEX GENETIC DISEASES

The NIAMS community is benefiting from another public-private partnership, the Genetic Association Information Network (GAIN). Since GAIN's inception, NIAMS investigators have been involved in its Collaborative Association Study of Psoriasis, an ambitious effort to combine genetic and clinical information from people affected by psoriatic skin disease and psoriatic arthritis. The project has yielded a wealth of data that researchers are using to develop diagnosis, treatment, and prevention strategies.

NIAMS-funded investigators have uncovered genetic susceptibility markers of alopecia areata and other autoimmune or auto-inflammatory skin and joint diseases, including lupus. Collaboration among United States and European researchers recently linked a component of the immune system and RA. At the NIH Clinical Center, sample collection has begun for a genomic analysis of Behçet's disease, a complex disorder of inflammation affecting skin, eyes, gastrointestinal tract, lungs, vasculature, and joints.

COLLABORATIONS AND TEAM SCIENCE

Behçet's disease is one of many conditions researchers are studying through the new NIH-wide Center for Human Immunology, Autoimmunity, and Inflammation. NIAMS' intramural program is taking a leadership role in the Center. Collaborations among scientists from several NIH Institutes who are studying related disease systems will facilitate studies about conditions associated with defective immune or inflammatory responses, and will allow them to apply their results to the development of interventions and, ultimately, disease prevention strategies.

In collaboration with orthopaedic surgeons at the Walter Reed Army Medical Center, NIAMS researchers recently discovered that tissue commonly discarded as waste contains special cells that feature many of the same properties as adult stem cells. The cells can be used for regenerative medicine, such as treating war-traumatized muscle, without subjecting patients to additional surgeries and related complications.

The NIAMS participates in the multi-Institute Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers program. In addition to conducting research, scientists at the Centers maintain core resources that all who are studying muscular dystrophy can use. A group of NIAMS-funded muscle researchers showed that defects in blood vessel constriction are associated with the severe fatigue that people with muscular dystrophy experience; mouse experiments suggest that com-

pounds with FDA-approval for other conditions may improve symptoms. Other scientists uncovered molecules that confer many of the benefits of exercise, at least in mice; the findings might lead to treatments for conditions that leave patients unable to exercise.

The scale and complexity of today's research problems and their solutions demand that the NIH explore new models for team science. In fiscal year 2008, the NIAMS started a program, Building Interdisciplinary Research Teams (BIRT), to promote partnerships among fields that share interests, but historically do not interact. Because collaborations proposed in the first round of applications suggested that modest investments in the program will provide great dividends, the NIAMS opened BIRT up to additional communities and expects to make another set of awards at the end of fiscal year 2009.

In the past year, the NIAMS has made considerable progress in leading a trans-NIH partnership with the National Aeronautics and Space Administration. By designating the U.S. portion of the International Space Station (ISS) as a National Laboratory, Congress underscored the significance that Americans place on the ISS' research potential. The NIH shares this belief and, for the next 3 years, will accept applications for studies that use the ISS for experiments directly related to the NIH goals of understanding human physiology and promoting the public's health.

CLINICAL STUDIES

One element of improving the Nation's health is to support clinical studies on which physicians can rely when discussing treatment options with patients. Before the Spine Patient Outcomes Research Trial (SPORT), many who had low back pain were conflicted about surgery. Now, patients can be assured that surgery relieves pain from herniated disks, but—if the pain is tolerable and not worsening—it will likely subside without surgery. Similarly, people who have pain due to spinal stenosis (a narrowing of the spinal column that occurs with age) are likely to benefit more from surgery than from noninvasive treatments such as physical therapy; but, they are not causing more damage if they adopt a "wait-and-see" approach before committing to an operation. Recently, SPORT offered guidance to help people who suffer from herniated disks personalize their treatment decisions by reporting that study participants who had surgery on an upper lumbar disk improved more than those with damage further down.

For decades, the NIAMS has invested heavily in efforts to understand fracture risk and to uncover strategies to prevent and treat bone loss. Although physicians now have an array of medications for people who are at risk of osteoporosis, many patients fail to benefit fully because they do not follow the treatment regimens. Because a method to improve compliance could immediately slow the growing health and economic burden that osteoporosis places on society, the NIAMS is funding research in this area.

CONCLUSION

The discoveries and activities highlighted above are just a few examples of research that will continue to benefit Americans from all walks of life. In partnership with Government and private entities, the NIAMS also develops and distributes science-based health information directly to patients, healthcare providers, and the public. The Institute will continue outreach to diverse populations through research, training, and information dissemination. Collectively, NIAMS programs have spurred understanding of many common, chronic, and costly diseases. Looking forward to the next decades, this progress provides a foundation for an era in which the burden of these debilitating conditions is reduced and—with time, continued support from the American public, and the dedication of our Nation's researchers—eliminated for millions of affected adults, children, and families.

PREPARED STATEMENT OF DR. RODERIC I. PETTIGREW, DIRECTOR, NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health. The fiscal year 2010 budget includes $312,687,000, which is $4,479,000 more than the fiscal year 2009 appropriation of $308,208,000.

The NIBIB is leading the development of revolutionary technologies that will help transform medicine in the United States and around the world. It has primary responsibility for uniting the engineering and physical sciences with the life sciences

to bring about new ways of thinking that will accelerate discovery and technology development. With a global vision and a public health mission, the Institute is working to develop technologies that enable personalized healthcare, early detection of disease, and treatments that are minimally invasive, cost-effective and widely accessible.

TRANSLATING TECHNOLOGY INTO PRACTICE

Ultimately, NIBIB seeks to expand the translation of technological advances into solutions that improve human health by reducing disease and enhancing quality of life. To accomplish this goal, NIBIB continues to fund bold and far-reaching projects that facilitate discovery and translate discovery to clinical practice. NIBIB-supported scientists in the innovative Quantum Grants Program are making extraordinary progress to develop new technologies and modalities for the diagnosis, treatment, or prevention of disease that will result in practical healthcare benefits for the Nation.

CHANGING HEALTHCARE DELIVERY THROUGH POINT-OF-CARE (POC) TECHNOLOGIES

Testing at the point of initial contact, or "point-of-care," rather than at specialized centers or hospitals utilizes state-of-the-art diagnostics and information systems that can be used in the doctor's office or even at home. Consequently, the use of POC devices can also help patients monitor their wellness in preventive medicine. The POC approach to health care delivery can significantly improve the quality and reduce the cost of health care by: providing earlier diagnosis of disease when treatment is more effective and less costly; making modern medicine available to those who lack access to regular care, such as people in rural settings or developing countries; combining cutting-edge diagnostic and communication technologies to bring patients into more frequent and regular contact with health care providers; and enabling a patient-centered process with home-based monitoring.

The NIBIB currently funds a network of four POC Technologies Research Centers that target the development of new POC technologies for early and rapid detection of strokes, detection of sexually transmitted diseases, rapid multi-pathogen detection for national disaster readiness, and diagnosis of infections that can be used in low-resource settings among underserved populations. Additionally, the NIBIB and the Department of Biotechnology (DBT) of the Ministry of Science and Technology of the Republic of India held a joint workshop on Low-Cost Diagnostic and Therapeutic Medical Technologies in November 2008 in Hyderabad, India. The workshop was a result of a bilateral agreement between the NIBIB and DBT to develop low-cost technologies to improve the quality of healthcare for underserved populations. Point-of-care testing is becoming a vital part of the world's healthcare delivery system, and is a key to reducing healthcare costs while maximizing accessibility for everyone.

HEALTH INFORMATION TECHNOLOGY

Health information technology research that enables the integration of clinical data, medical image diagnostic and treatment data with the patient's medical history in a comprehensive electronic medical record will improve clinical decision-making. The ability to connect and exchange diagnostic information and medical images between healthcare providers, clinics, and hospitals will help provide the timely information that is needed for effective healthcare and will help reduce unnecessary, excessive, and duplicative procedures. A patient-centered approach to comprehensive electronic health records will allow patients access to their health information. This will enable patients to play an active role in their own wellness by enabling them to ask knowledgeable questions about treatment options. Additionally, patients are also empowered to provide this information to any and all healthcare providers as needed, independent of their location or where the medical data was created or stored. The NIBIB supports research in new technologies to address issues such as: interoperability of data systems, compatibility of computer software across medical institutions; security of data during transmission; HIPPA compliance; and availability of affordable data systems for patient care providers.

MICROCHIP CAPTURES EARLY CIRCULATING CANCER CELLS

NBIB's budget request and its research projects are consistent with the President's multi-year commitment for Cancer. Malignant cancers shed cells that enter the circulation, travel to other areas of the body, and often grow into secondary tumors, or metastases. Indeed, metastases are responsible for the great majority of cancer deaths. It is estimated that 70,000 men per year are diagnosed with recur-

rent prostate cancer after prostatectomy, as shown by rising prostate surface antigens. For these men, the ability to detect and characterize the malignant cells in the blood may enable personalized therapy. Researchers are developing a technology to facilitate quantitative detection of circulating tumor cells (CTCs). They have engineered a microchip with a large surface area of an adhesion molecule that binds CTCs from whole blood, making detection of CTCs more reliable than previous approaches. They are analyzing molecular and genomic information in the CTC's to identify new biomarkers to customize treatments that are personalized for the patients and to predict treatment outcomes. The NIBIB-supported research has the potential to eliminate or greatly reduce cancer deaths due to metastases.

REGENERATING BRAIN TISSUE TO PROMOTE STROKE RECOVERY

Brain cells can be irreversibly damaged in a matter of minutes when the blood supply carrying oxygen and glucose is interrupted in a stroke. Individuals who have had a stroke may experience partial paralysis or problems with awareness, attention, learning, judgment, memory, or speech. An international team of researchers from Baylor College of Medicine, Rice University, London's National Institute of Medical Research, King's College of London, and Edinburgh University is integrating cutting-edge imaging, biological, and engineering techniques to map and understand normal brain regions that are responsible for generation of new neurons in the adult. The ultimate goal is to bioengineer a cellular system mimicking these brain regions that can eventually be used to replace and/or drive repair of stroke-damaged tissue.

MINIATURE ARTIFICIAL KIDNEY REPLACES TRADITIONAL DIALYSIS

Nearly one-half of a million people in the United States suffer from end-stage renal disease (ESRD), and the incidence rate of this disease has been steadily increasing for over 25 years. Kidney transplantation provides the best option for ESRD patients, but a shortage of donors means that most patients never make it to the top of a waiting list. The alternative is dialysis, which is expensive, inconvenient, far less effective, and significantly lowers the patient's quality of life. An interdisciplinary group of researchers has envisioned a way to improve management of ESRD by developing an implantable, self-regulating, bioartificial kidney capable of filtering toxins from the blood as well as replacing some of the metabolic functions of a healthy kidney. Such an implantable bioartificial kidney could substitute for transplantation and will truly be a quantum leap in healthcare, giving hope, independence, and mobility to the 350,000 patients presently tethered to thrice-weekly in-center dialysis.

INSULIN-PRODUCING CELLS FROM AMNIOTIC FLUID STEM CELLS TREAT DIABETES

More than 1 million people in the United States suffer from type 1 diabetes, which is caused by the destruction of insulin-producing pancreatic islet cells. Currently available insulin therapy by itself does not cure the disease or prevent many of its long-term complications. Transplantation of islet cells has shown promise, but there is a shortage of donors, and the process is expensive, inefficient, and requires life-long immunosuppression. Researchers from Wake Forest University and the University of Miami have combined their expertise in stem cell differentiation and in vivo islet cell transplant studies to explore a new approach using amniotic fluid stem cells. The team has successfully isolated amniotic fluid stem cells and generated insulin-producing, islet-like cells in vitro. Future work will determine whether these cells are able to function and survive in animal models of diabetes. If successful, this approach could potentially provide a curative treatment for type 1 diabetes through transplantation using cells produced from amniotic stem cells.

MOLECULAR THERANOSTICS: NEW TECHNOLOGIES FOR THE DIAGNOSIS AND TREATMENT OF DISEASES

The concept of combining a therapeutic with a diagnostic agent is rapidly evolving and goes beyond traditional diagnostic tests that screen or confirm the presence of a disease. With specialized molecular imaging techniques and biomarkers, theranostics might predict risks of disease, diagnose disease, and monitor therapeutic response leading to real-time, cost-effective treatment. NIBIB supports a number of teams that are developing novel theranostics and approaches that can be applied in clinical studies of human patients. A team of chemists and neurosurgeons at the University of Michigan is developing highly specific, dye-loaded nanoparticles capable of delivering targeted photosensitizers to improve the survival of brain tumor patients. This technique will allow neurosurgeons to visualize the

brain tumors for surgical resection of the main tumor mass while eradicating remaining tumor cells through a process known as photodynamic therapy. These particles also contain imaging contrasting agents to visualize response to therapy.

PREPARED STATEMENT OF DR. NORA D. VOLKOW, DIRECTOR, NATIONAL INSTITUTE ON DRUG ABUSE

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute on Drug Abuse (NIDA) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $1,045,384,000, which is $12,625,000 more than the fiscal year 2009 appropriation of $1,032,759,000.

Drug abuse and addictions are preventable conditions, yet continue to cause immeasurable human suffering, with associated societal costs estimated to exceed one-half a trillion dollars annually in the United States. Tobacco use alone is responsible for more than 400,000 deaths per year, and is the leading cause of preventable death in the United States. NIDA's budget request and its research projects are consistent with the President's multi-year commitment for cancer. For example, NIDA has active programs to hasten the development of new, more effective treatments for nicotine addiction that can dramatically reduce the prevalence of diseases like lung cancer and emphysema, which mean an early death for many smokers. Other NIDA-supported research advances have contributed to steady declines in both licit and illicit drug use over the years, particularly among our Nation's youth. Our latest Monitoring the Future (MTF) survey of drug use patterns and trends among 8th, 10th, and 12th graders reveals, for example, that tobacco use has declined continuously since its peak in the mid-1990s, and is presently at its lowest level since the first MTF survey in 1975. However, if we are to fully eradicate drug abuse and addictions, we must find novel approaches to prevent drug abuse (including smoking) among the significant fraction of youth who, because of strong genetic and/or environmental propensity, appear refractory to current efforts. Additional challenges include the growing abuse of prescription medications, including opioid analgesics (e.g., painkillers), stimulants (e.g., ADHD medications), and CNS depressants (sleep and anxiety medications). NIDA is committed to closely monitoring these trends and to furthering the development of innovative strategies to counter them, including the widespread dissemination of screening and early intervention tools for medical settings to increase the medical community's participation in identifying and treating substance abuse disorders.

ADDICTION MEDICATIONS: CHANGING THE CULTURE OF TREATMENT

NIDA's accelerating rate of discovery is beginning to spur the advent of better medications and behavioral interventions to counteract drug-induced changes in brain function. Among the strategies NIDA supports for medications development are those to: counter stress responses, which frequently trigger relapse to drug use; strengthen executive function and inhibitory control so that drug abusers can better control their urge to take drugs; and interfere with drug-conditioned memories to prevent relapse when drug abusers are exposed to environments they associate with drug use. Other research includes development of vaccines, or antibody-based approaches, which can block both illicit and licit drugs (e.g., nicotine) from ever reaching the brain, thereby inhibiting their rewarding effects. In the context of nicotine addiction, this approach may help prevent smokers from escalating to addiction and/or facilitate abstinence in those who seek to quit. It also complements ongoing efforts to discover new, more effective medications through conducting screens of novel compounds and chemical libraries and applying promising findings to help people achieve abstinence from tobacco and other addictive substances.

To accelerate progress in combating substance use disorders, there must also be social change to recognize that people who suffer from addiction require medical treatment. Presently, addiction treatment occurs largely outside of mainstream medicine, even though drugs undermine overall health, frequently appearing alongside other medical and psychiatric conditions. To help change this culture, NIDA is providing knowledge of associated brain dysfunctions and developing and deploying effective addiction medications. As these efforts succeed, the consequent medicalization of drug abuse and addiction will allow (1) clinicians to respond to their patients' needs more effectively and in a more personalized fashion; (2) insurance companies to become increasingly responsible for the coverage of treatments that can dramatically improve overall health; and (3) pharmaceutical companies to be incentivized to develop novel addiction medications. As the stigma of addiction wanes, the dissemination of proven treatments will expand to include the popu-

lations that need them the most, such as those involved in the criminal justice system, half of whom meet the criteria for drug abuse or dependence, according to estimates from the Department of Justice. Broader treatment access for drug-addicted offenders will help them to successfully transition back into society, dramatically reducing not just drug abuse, but also criminal recidivism.

GENES AND ENVIRONMENT: HIGH PAY-OFF RESEARCH

A steady flow of genetic discoveries is uncovering previously unsuspected genes whose products may be involved in the addiction process and therefore present good candidates for medication development. They also herald the advent of more personalized interventions based on a patient's genetic profile. And, because genes influence both vulnerability and resilience to substance abuse and other mental disorders, genetic data will further our understanding of the basic mechanisms underlying the disease of addiction, as well as its frequently associated comorbid conditions.

But genes do not act in isolation; rather, they work in tandem with developmental and environmental factors to determine a person's drug abuse vulnerability. Therefore, NIDA is encouraging more research to understand how genes might mitigate or amplify social influences that affect individual choices and behaviors related to substance abuse. Conversely, environmental elements, such as parenting quality, home conditions, stress, diet, pollutants, and, of course, exposure to drugs of abuse, can regulate gene expression. Uncovering the mechanisms behind these so called epigenetic effects, offers a path to alleviate and perhaps even override a genetic predisposition by adjusting environmental variables.

One approach NIDA is pursuing is the merging of genomic and brain morphology (i.e., brain structure) data in order to understand how genes influence human brain development. Such data would be invaluable as a basis for understanding the contribution of specific genes to neuropsychiatric disorders and how exposure to certain environmental factors can trigger disease in those who are genetically vulnerable. This research would, in turn, open the door to next-generation pharmaceuticals that could target and perhaps even prevent or reverse disease processes. The recent discovery of histone demethylases—a new family of genome modifying enzymes—is just one example of a set of proteins that could be targeted for medications development.

Also critical to substance abuse prevention and treatment is the development of reliable assays for drug exposure and addiction vulnerability. Although tests of bodily fluids or hair and surveys using self-report questionnaires are used routinely, their value is compromised by their limited reliability, low sensitivity, and narrow scope. NIDA will encourage research to find reliable biomarkers—or indicators of a biological response/vulnerability to drug exposure—for assay development. The ability to quantify thousands of biomarkers in a consistent, expeditious, and affordable manner will yield revolutionary new approaches to the prevention and personalized treatment of substance abuse.

THE RELEVANCE AND IMPACT OF COMORBID CONDITIONS

NIDA research has demonstrated that drug abuse cannot be treated in isolation from associated concerns, such as criminal behavior, mental and physical health status, social functioning, and HIV/AIDS. A robust and consistent effort to tap into and integrate different sources of knowledge will be needed to design and implement effective interventions in the future. This will be particularly important for members of the military and their families, who may be facing difficult challenges related to substance abuse in the coming years. Many are returning from active duty with post-traumatic stress disorder (PTSD) and/or chronic pain conditions, both of which can be comorbid with drug abuse and require comprehensive treatment interventions. In response to these projections NIDA will increase our research investment in this area and collaborate with the Veteran's Administration, the Substance Abuse and Mental Health Administration (SAMHSA), and other NIH Institutes—NIMH, NCI, NIAAA, and NHLBI—in developing a responsive and forward-looking research agenda.

UNDERSTANDING THE DYNAMICS OF DRUG ABUSE AND HIV

NIDA's recent revamping of its HIV/AIDS research strategy better addresses the critical need for new therapies for drug abusers with HIV and for research designed to uncover more about the complex medical consequences, such as neuroAIDS. Initiatives in this area will help elucidate the effects of genetic variations on disease progression, and on how drugs of abuse and medications (for drug addiction and HIV) interact with both host and viral genes. To further such innovations, NIDA has established the Avant-Garde Award for exceptionally creative researchers offer-

ing transformative approaches to major challenges in biomedical and behavioral research on drug abuse and HIV/AIDS. Awardees are undertaking diverse approaches, such as evaluating the effectiveness of expanded access to highly active antiretroviral therapy in decreasing new cases of HIV infection among injection drug users. Evidence to date suggests the utility of this approach for injection drug users and their partners; if widely adopted, it could also help stem the HIV epidemic around the world. In addition, NIDA is promoting research on HIV screening and on how to best integrate testing and counseling into drug abuse treatment settings, among criminal justice populations, and in other countries that have been hit especially hard by the epidemic. Learning one's HIV-positive status reduces risk behaviors and, when linked to HAART, makes the person a less efficient vector for spreading the disease.

In sum, the health of our Nation and its leadership role in bringing science to bear on drug abuse and addiction depend on our ability to continue to support promising biomedical research that can bring with it enduring and transformative public health changes not just to this country but to the rest of the world. Thank you for this opportunity, and I will be pleased to answer any questions you may have.

PREPARED STATEMENT OF DR. JAMES F. BATTEY, JR., DIRECTOR, NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute on Deafness and Other Communication Disorders (NIDCD) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $413,026,000, which is $5,767,000 more than the fiscal year 2009 appropriation of $407,259,000.

The NIDCD conducts and supports research and research training in the normal and disordered processes of hearing, balance, smell, taste, voice, speech, and language. Last year, NIDCD celebrated its 20th anniversary. Over the past two decades, extraordinary research opportunities have led to scientific breakthroughs in the study of genes, proteins, sensory and supporting cells, and molecular processes that directly affect our understanding of communication disorders. NIDCD-supported scientists have also made substantial progress in behavioral studies that increase our understanding of how communication processes impact health. NIDCD's budget request and its research projects are consistent with the President's multiyear commitments to cancer and autism research. The following are notable research highlights built upon two decades of NIDCD support.

HAIR CELL REGENERATION

Our ability to hear relies on sensory cells in the inner ear, called hair cells. Hair cells can be damaged by disease, injury, aging, or exposure to certain drugs. When enough hair cells are damaged, an individual experiences hearing loss. Although fish, amphibians, and birds can spontaneously regenerate new hair cells to replace damaged ones, mammals (including humans) cannot. NIDCD-supported research into the development of the mammalian inner ear has led to a better understanding of which cells in a developing embryo become hair cells, and which become supporting cells that help maintain the hair cells. These basic studies have provided the foundations for more recent advances. For example, NIDCD-supported scientists have identified specific genes that determine an inner ear hair cell's fate. Building on these studies,

NIDCD-supported scientists were able to regenerate new hair cells in laboratory mammalian animal models, and restore hearing in some cases. These promising results provide hope that we might someday be able to regenerate functioning hair cells in humans.

PREVENTING NOISE-INDUCED HEARING LOSS

Prevention of noise-induced hearing loss is another important goal for the NIDCD. Approximately 15 percent of Americans between the ages of 20 and 69—an estimated 26 million American adults—have high-frequency hearing loss caused by exposure to loud sounds or noise at work or during leisure activities. Since the sensory hair cells of the inner ear do not spontaneously regenerate in humans, preventing noise damage to these cells is critical for long-term health. In October 2008, NIDCD launched a new public education campaign called "It's a Noisy Planet. Protect Their Hearing." The campaign is designed to increase awareness among parents of children ages 8 to 12—or "tweens"—about the causes and prevention of noise-induced

hearing loss. With this information, parents and other adults can encourage children to adopt healthy habits that will help them protect their hearing for life.

IMPROVING TECHNOLOGIES TO TREAT HEARING LOSS AND BALANCE DISORDERS

The NIDCD supports many research efforts to develop or improve technologies for the treatment of hearing loss and balance disorders. The cochlear implant is an electronic device that provides a sense of sound to individuals who are profoundly deaf or severely hard-of-hearing. Cochlear implants process sounds from the environment by directly stimulating the auditory nerve, bypassing the malfunctioning cells in the inner ear. Sustained NIH support has greatly improved this technology so that, with the appropriate training and support, deaf and severely hard-of-hearing individuals who receive a cochlear implant can enjoy an enhanced quality of life by participating more fully in society. Currently, cochlear implants are most successful in children who receive them at a young age, when the brain is still in an active phase of language development. NIDCD-supported scientists are investigating the benefits of bilateral cochlear implantation, in which a cochlear implant is fitted into both ears. Results show that individuals receiving two cochlear implants are significantly better at localizing sounds and hearing speech in a noisy room compared to individuals with one implant. In addition, within 1 to 2 years after implantation, children with two cochlear implants will have learned how to locate sounds, and most will be able to localize sounds better than children with only one implant.

Much like hearing, our sense of balance relies on hair cells arranged in specialized structures within the inner ear, which together make up our vestibular system. Vestibular hair cells are susceptible to damage by the same mechanisms as hearing hair cells—drugs, trauma, and infection—and their dysfunction can lead to dizziness or balance problems. Building on lessons learned from cochlear implant research and technology, NIDCD-supported scientists are now working to develop an implanted device to help partially restore a person's sense of balance. Although the prototype vestibular implant is still being used in animal studies, it has the potential to benefit more than 90 million Americans who experience dizziness or balance problems in the future.

NIDCD also actively supports research to improve hearing aid technology. Improving hearing in noisy environments is a major challenge for hearing aid users. Of the currently available technologies, directional microphones that focus on nearby sounds and filter out sounds further away show the most promise for addressing this problem. NIDCD-supported scientists have successfully completed a prototype of a low-power, highly directional microphone that is modeled on the acute directional hearing of a parasitic fly and is small enough to fit into a hearing aid. The device could offer hearing aid users significant improvement in their ability to listen to conversations amidst background noise. NIDCD's goal is for this research is to lead to the development of hearing aids that are more personalized and better able to restore normal hearing.

IDENTIFYING GENES RESPONSIBLE FOR COMMUNICATION DISORDERS

NIDCD-supported scientists are identifying and describing genes involved in many communication disorders, including autism, dyslexia, stuttering, speech-sound disorders, and hearing loss. Currently, scientists have mapped more than 80 genes responsible for inherited hearing loss. Starting in fiscal year 2009, NIDCD is serving as the lead Institute for an NIH Government Performance and Results Act (GPRA) goal to "identify or study additional genes involved in communication disorders in human and animal models by 2011." To achieve this goal, NIDCD- and other NIH-supported scientists are using the knowledge gained from the Human Genome Project to identify genes that play a role in communication disorders. These efforts will inform scientists as they develop genetic tests to predict communication disorders and personalize treatment plans for individuals affected by them. In a recent study, NIH-supported scientists scanned the human genome for genetic differences between individuals with and without autism. They identified both common and rare genetic factors that affect the risk for developing autism spectrum disorders (ASD). The results suggest that there are specific inherited genes that can cause abnormal connectivity between nerve cells in the brains of people with an ASD. These abnormal connections may be, in part, responsible for their communication difficulties.

AUTISM AND LANGUAGE

According to the American Psychiatric Association, approximately 20–40 percent of individuals with autism spectrum disorders have apparently normal intellectual abilities and relatively intact language skills, but they still have difficulty with the

social aspects of communication. These individuals are categorized as having high-functioning ASD. In order to develop useful and appropriate treatment programs for them, scientists need to know what specific aspects of communication are most impacted. NIDCD-supported scientists have used standardized conversational tests to compare individuals with high-functioning ASD to age-matched individuals without ASD. These comparisons enabled them to identify three main areas of conversational difficulty for individuals with high-functioning ASD: (1) Managing topics—responding in a way that is pertinent to the topic and identifying topics of interest to both parties; (2) Managing information—understanding how much information is enough and knowing what type of information to provide; and (3) Establishing reciprocity—participating in a balanced back-and-forth exchange. Researchers can now use these results to develop personalized treatment programs targeted to improve existing conversational skills and build new skills in the areas of communication that are most affected in individuals with high-functioning ASD.

VOCAL FOLD REGENERATION

The vocal folds—also referred to as vocal cords—are two elastic bands of tissue located in the larynx, or voice box, directly above the trachea, or windpipe. The vocal folds produce voice when air held in the lungs is released and passed through the partially closed vocal folds, causing them to vibrate. Vocal fold scars can result from injury or inflammation, or because of surgery to remove vocal fold nodules or polyps. The scars increase vocal fold stiffness and reduce their ability to vibrate. An individual with scarred vocal folds may have a hoarse, breathy, or low-pitched voice. NIDCD-supported scientists have developed a new class of soft gel material to serve as a scaffold to encourage regeneration of vocal fold tissue. Specific particles within the material can also be modified to bind and slowly release therapeutic drugs within the vocal folds as a way to further encourage regeneration of the tissue. This new material is currently being tested to learn what types of changes, such as particle size, distribution, and so on, will optimize tissue regeneration. Once the gel is optimized in laboratory tests, it may offer a potential future personalized treatment for individuals whose vocal folds have been damaged due to scarring.

Mr. Chairman, I would like to thank you and members of this subcommittee for giving me the opportunity today to present examples of scientific advances made with the support of the NIDCD. I am pleased to try to answer your questions.

PREPARED STATEMENT OF DR. LAWRENCE A. TABAK, DIRECTOR, NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Dental and Craniofacial Research (NIDCR) of the National Institutes of Health. The fiscal year 2010 budget includes $408,037,000 which is $5,385,000 more than the fiscal year 2009 appropriation of $402,652,000.

FACING THE FUTURE

Extraordinary advances have been made in recent years at the interface of traditional scientific disciplines. Multidisciplinary teams of scientists, engineers and clinicians have combined advances in biochemistry, cell and molecular biology, engineering, genetics, and neuroscience to gain a deeper understanding of the mechanisms underlying disease pathogenesis. This has yielded clues for the prediction of those most at risk for disease, approaches to personalized interventions, and strategies to prevent disease progression.

For example, who has not marveled at the complexity of a face? Or how nature designed the mouth and its unique soft and hard tissues as a gateway to the body and, in some creatures, a first line of defense? Among Nature's greatest miracles of design and engineering is the craniofacial complex. Utilizing the many powerful research techniques and tools now available, teams of NIDCR-supported scientists are creating a publicly accessible informatics platform, termed FaceBase, that will enable multiscale analysis of all aspects of craniofacial development. This basic understanding is key to one day preventing and more effectively managing craniofacial defects and disorders. Each year thousands of infants are born with a variety of craniofacial dysmorphologies. While many of these conditions, such as cleft lip and/or palate can be managed surgically and with supportive therapies, others are more challenging to treat. For example, children born with ectodermal dysplasias must deal with either malformed or multiple missing teeth.

The NIDCR's new strategic plan captures the communal spirit required to address complex oral and craniofacial diseases and conditions. It lays out the challenges of the immediate road ahead for dental, oral, and craniofacial research—challenges that our 2010 budget positions us to meet. But above all, our plan lays out the great promise that awaits scientists and the American public in the years ahead.

WIDEN THE SCOPE OF INQUIRY

As the volume of biological information has grown, so, too, have the questions that scientists can ask. No longer must the human body be neatly subdivided into its constituent parts and studied in strict isolation, one organ from another. Biological clues in one part of the body often have application elsewhere in the body.

An excellent example is oral cancer which results in more than 7,500 deaths each year in this Nation. Unlike cancers that arise in the internal organs, tumors of the oral cavity are often readily accessible for biopsy and prompt study. This has allowed a dedicated corps of scientists to make tremendous inroads into defining the molecular errors that trigger the disease. For example, a key signaling pathway, termed Akt-mTOR, is frequently dysregulated in head and neck carcinomas. Their research efforts not only will improve the diagnosis and treatment of oral cancer, it also will provide comparative data and possible new leads for scientists who study other less accessible tumors.

The same is true of research on the microbial biofilm that forms on the hard and soft tissues of the mouth. Oral health researchers have defined more than 600 microbes that inhabit the mouth and have spent generations studying the communal dynamics that contributes to common diseases, such as periodontal disease and tooth decay. This decades-long head start will help to guide research now under way on the other biofilms that form throughout the body. This line of study emerges from the growing recognition that subtle shifts in the composition of the body's biofilms may play a major contributory role in myriad human diseases. Advances are being enabled by powerful new technologies that allow for the more facile sequencing and analysis of microbial genomes. Indeed, microbes that have not yet been cultivated are now amenable to study, in silico, which helps describe the lifestyle of each organism.

NIDCR intends to make considerable investments in genome wide association studies of diseases and conditions affecting the craniofacial complex that will also inform pathology in other regions of the body. For example, an analysis of genes associated with Sjögren's syndrome, an autoimmune disease affecting 1 million or more Americans, will likely provide clues for other diseases such as rheumatoid arthritis or systemic lupus erythematosus. Chronic facial pain, including temporomandibular joint and muscle disorders, has begun to yield its secrets to the efforts of geneticists and neuroscientists. Particularly important are efforts to better understand the transition of acute to chronic pain. Compelling evidence suggests this may be related to neural plasticity, in a manner not dissimilar to mechanisms that underlie memory.

These are but a few of the cross-cutting issues that are now on NIDCR's research agenda. To investigate them vigorously, the NIDCR must continue to encourage innovation and bring to bear the best science possible. But therein lays another challenge.

KEEP THE PIPELINE STRONG

For the Nation's oral health community to tackle NIDCR's ambitious research agenda successfully, it needs tight integration among research, practice, and education. This synergy holds the key to solving the many disorders that affect the oral and craniofacial complex. During 2010, the Institute will continue to emphasize training and career development for oral health professionals, to ensure that we increase a thriving community of dentist-scientists ready to capitalize on the rapid and significant advances occurring in biomedical and behavioral research. At the same time, the Institute must continue to attract scientists from outside its traditional research arenas. We will need to cover all of the scientific bases, from chemists and computer scientists to molecular biologists and mathematicians. All play critical roles and will be invaluable in ensuring that the best science moves rapidly into clinical studies. In an effort to strengthen the pipeline at every stage, the NIDCR is determined to maintain its high level of commitment in 2010 to funding new and early-stage investigators in a wide range of scientific fields.

PROMOTE CLINICAL INNOVATION

Moving forward in the clinical realm will require a great deal of innovative thinking. In 2010, NIDCR will continue to lay the foundation for the next great revolu-

tion in oral healthcare: biology-based dental care. As the name suggests, dentistry will launch molecular-based healthcare over the next several decades. Using salivary-based diagnostics, this new oral health paradigm will provide patients with more precise diagnoses and a greater opportunity to practice prevention. Greater understanding of disease pathogenesis and the variation in individual susceptibility will yield targeted and personalized therapies to treat their conditions more efficiently. This will provide a better chance to maintain their teeth and supporting bone ultimately leading to a lifetime of high-quality health.

To catalyze adoption of these advances, and to further the evidence base of the dental profession, in 2010, the NIDCR will continue to support its Practice Based Research Networks initiative, which now engages hundreds of dentists nationwide in scientific studies.

ADDRESS HEALTH DISPARITIES

As beneficial as biology-based dental care will be one day in improving the oral health of Americans, every effort must be made, now and in the future, to combat oral health disparities. Millions of primarily low-income Americans have yet to benefit fully from advances in dental care, including countless children and their families.

The fiscal year 2010 budget request will allow the NIDCR to maintain strong support for its Centers for Research to Reduce Health Disparities. These Centers continue to demonstrate the value of partnering with communities throughout the research process in order to gain a complete understanding of the factors contributing to dental disease in each community and to develop appropriate intervention strategies. Emerging from this initiative will be a greater focus to identify the many complex factors that contribute to the disparities, targeted, multi-tiered research to address the problem, and coordinated efforts to promote greater awareness of oral disease.

The Institute also plans to continue partnering with the Centers for Disease Control and Prevention to monitor the status of the Nation's oral health. As a part of this effort, the NIDCR will seek to validate new methods to measure and document oral, dental, and craniofacial diseases.

DENTAL CARE IN THE FUTURE

Biology-based dental care will transform the most fundamental principle of the profession: restoration of form and function. No longer will dentists rely as readily on mechanical instruments and ceramo-metallic materials to repair damaged tissue. They will regenerate form and function (a) using the precision of molecular information—or the underlying cause of the disease—as their operational guide and (b) employing the body's own cells and biochemistry as their engineering materials.

Future dentists will possess more powerful optical instruments to visualize and accurately characterize whether near microscopic losses of mineral from a tooth surface will be self-correcting or whether they will progress to full blown decayed lesions. Advances in imaging, genomics and proteomics will allow a clinician to profile the circuitry of a tumor cell biopsied from the mouth. This diagnostic work-up will guide the choice of chemotherapy drugs to those that are most likely to target the internal wiring of the tumor cell and kill it. Targeted treatments will allow the removal of only the cancerous tissues.

In closing, and as highlighted in our 2010 budget justification, the NIDCR will continue to invest in research and research training to meet emerging scientific opportunities and challenges. This budget request will enable us to work towards achieving the four goals outlined in our strategic plan. These goals are attainable, and in striving to meet them, we can realistically expect to improve the Nation's oral health for generations to come.

PREPARED STATEMENT OF DR. GRIFFIN P. RODGERS, DIRECTOR, NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Mr. Chairman and members of the subommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $1,781,494,000, which is $20,156,000 more than the fiscal year 2009 appropriation of $1,761,338,000. Complementing these funds is an additional $150,000,000 also available in fiscal year 2010 from the special statutory Type I Diabetes Research Program for NIDDK.

Our Institute supports research on a wide range of common, chronic, costly, and consequential health problems that affect millions of Americans. These include diabetes and other endocrine and metabolic diseases; digestive and liver diseases; kidney and urologic diseases; blood diseases; obesity; and nutrition research. Additionally, consistent with the President's commitment to increase funding for cancer research, and with the HHS-wide initiatives on autism, NIDDK will support research relevant to these diseases.

GENETIC FACTORS IN COMPLEX DISEASES

Many complex diseases within the NIDDK mission result from interactions amongst multiple genetic and environmental factors. Building upon the wealth of genetic information from the Human Genome Project, basic research on genetic contributors to these diseases lays the foundation for translation of knowledge into clinical settings, where it can be used to better predict and pre-empt disease development, as well as provide more personalized medical care.

For example, the NIDDK supported recent research uncovering six new genetic variants involved in type 2 diabetes. Combined with previous genetic findings, this new knowledge can help to determine who is at risk for this disease and how it might best be treated and prevented. NIDDK research has also recently shown how a genetic variant associated with type 1 diabetes works to alter immune function, enhancing understanding of this disease and highlighting potential targets for therapy. NIDDK also contributed to international research efforts yielding an explosion of new genes or gene regions associated with the inflammatory bowel disease known as Crohn's disease. The total number of known susceptibility genes currently stands at more than 30, each of which promises fresh insights into this disease and its management. Genetic analyses have also identified contributors to other diseases within the NIDDK mission, including nonalcoholic fatty liver disease, liver cancer, and diabetes-related kidney disease. Some of this research addresses populations disproportionately affected by certain diseases. For example, genetic variants were identified that account for much of the burden of nondiabetic kidney disease in African Americans. These studies may lead to future screening strategies and more personalized therapies.

The NIDDK also participates in trans-NIH efforts exploring how genetic factors impact disease. Data from an NIDDK-sponsored study of the genetics of diabetic kidney disease are being analyzed by the Gene Association Information Network to inform disease prevention, diagnosis, and treatment. The NIDDK leads two projects within the Genes, Environment, and Health Initiative, which studies effects of genetic variants on disease risk in response to environmental exposures. The NIH Roadmap Epigenomics Program is researching how epigenetics—or biochemical changes to DNA—can control genes during different stages of development, such as fetal epigenetic responses in the intrauterine environment and the risk of diabetes after birth.

CLINICAL AND POPULATION-BASED RESEARCH

Clinical and population-based research generates important information not only for developing more effective therapies, but also for identifying strategies to pre-empt disease development—both essential for the future of medical care. NIDDK-sponsored research informs screening efforts to detect early signs of susceptibility and prevent full-blown disease. For example, recent studies have proven the potential of intensive early colonoscopy screening for precancerous polyps in African Americans to reduce their disproportionate colon cancer burden.

NIDDK-sponsored efforts are also testing interventions to address type 2 diabetes related to overweight in both adults and children. Researchers are studying obese adults with type 2 diabetes to observe the effects of lifestyle changes to lower risk of diabetes complications. Similarly, in children, a study is determining if healthier food choices in schools, increased physical activity, and improved awareness of healthy behaviors can reduce weight and lower risk factors for type 2 diabetes—a disease that was once seen only in adults, but has been increasing in American youth.

Obesity continues to be one of our Nation's most pressing health problems. The NIDDK supports a multi-pronged obesity research effort that includes studies of molecular and environmental contributors to feeding behavior and metabolism, processes such as inflammation in metabolic tissues, bariatric surgery and other potential treatments for obesity, and lifestyle interventions to prevent or reverse obesity. For example, a recent study showed that modest reductions in time spent by children watching TV or using the computer have beneficial effects on their weight.

Clinical research is also yielding new insights into the development and management of kidney, urologic, and liver diseases. Recent clinical studies showed the limited effectiveness of drugs to enable vascular access during hemodialysis for kidney failure and for treating chronic kidney disease due to high blood pressure in African-American patients. A multi-center network is investigating causes of the two most common urologic pelvic pain disorders-interstitial cystitis/painful bladder syndrome and chronic prostatitis/chronic pelvic pain syndrome—which may yield new targets for managing these diseases. A new clinical research network conducting translational research on chronic hepatitis B is focused on understanding disease processes and applying this knowledge to more effective treatment and control strategies.

ENHANCING FUTURE HEALTH RESEARCH

The biomedical research enterprise will depend heavily on the next generation of investigators, innovative ideas of individual scientists, and the synergy of public-private partnerships. The NIDDK, along with the wider NIH, will continue its commitment to helping new investigators realize their potential through such efforts as special funding consideration, small grant and career awards, and mentoring workshops. The Institute also remains firmly committed to supporting investigator-initiated research. Public private partnerships through such entities as the foundation for the NIH will continue to expand the reach of NIDDK research.

Strategic planning, analyses of disease burden, and research coordination are tools utilized by the NIDDK to advance research. Recently, the National Commission on Digestive Diseases—for which NIDDK provided leadership and support—released its long-range research plan, identifying challenges and opportunities for digestive diseases research. A separate report on the burden of digestive diseases in the United States was prepared by the NIDDK to inform this research plan. The "NIDDK Prostate Research Strategic Plan," released in 2008, provides recommendations for future research efforts targeting the causes, prevention, and treatment of benign prostate disease.

NIH recently initiated an effort to update its 2004 "Strategic Plan for NIH Obesity Research" in order to review research progress and identify new opportunities. This strategic planning effort is overseen by the NIH Obesity Research Task Force, which I co-chair together with Dr. Elizabeth Nabel, Director of the National Heart, Lung, and Blood Institute.

Coordination to enhance research efforts across the NIH and with research partners in other Federal agencies is also achieved through the work of coordinating committees. The Diabetes Mellitus Interagency Coordinating Committee (DMICC) coordinates diabetes activities across the Federal Government and fosters opportunities for agency collaboration. In its coordinating role, the DMICC encourages Federal research collaborations, minimizes overlap of agency research efforts, and enhances public awareness of diabetes research and health information provided by Federal agencies. The DMICC is the focal point for diabetes research planning efforts.

PROMOTING HEALTH AWARENESS

In addition to supporting health research, the NIDDK remains committed to ensuring that knowledge gained from research is used to promote health awareness. Relevant activities include the National Diabetes Education Program, National Kidney Disease Education Program, Weight-control Information Network, Celiac Disease Awareness Campaign, and programs to promote prevention of obesity and overweight.

Recently, the NIDDK expanded its health information materials with a new Awareness and Prevention series of fact sheets. These publications are designed to raise awareness of diseases such as diabetes, digestive diseases, and kidney and urologic diseases among people not yet diagnosed with these illnesses. Materials produced by the NIDDK are often translated into multiple languages. For example, the Institute is currently developing Asian language materials on hepatitis B to reach people whose origins place them at higher risk—a priority highlighted at the NIH Consensus Development Conference on Management of Hepatitis B in October 2008.

Another resource for promoting health awareness in affected groups is a set of teaching tools for school-based diabetes education in American Indians, who have the highest rates of diabetes in the United States. Through educating American Indian youth about diabetes prevention, these tools aim to reduce the incidence of type 2 diabetes in these young people and their families, as well as encourage entry into health-related careers.

CLOSING REMARKS

A key goal of the NIDDK is to maximize the return on research investments to derive the greatest health and economic benefits. Embedded in the population-based projects I mentioned is a consideration of their cost-effectiveness. As areas of research converge around common disease mechanisms—such as microbial influences on health—and research tools—like genetics-based technologies—opportunities exist to leverage resources and foster collaborations. Past investments in sample repositories and databases can be extended in ancillary and follow-up studies. In these ways, the intrinsic economic benefit of NIDDK-sponsored research can be fully realized.

In closing, I thank the chairman and members of the subcommittee for this opportunity to highlight some of the NIDDK's research and outreach efforts to improve our Nation's health. I would be pleased to answer any questions you may have.

PREPARED STATEMENT OF DR. LINDA BIRNBAUM, DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health. The fiscal year 2010 budget includes $684,257,000, which is $21,437,000 more than the fiscal year 2009 appropriation of $662,820,000.

INTRODUCTION

NIEHS works at the forefront of public health to meet the challenges the field of environmental health sciences faces in the 21st century. Meeting these numerous and demanding challenges is vital to reducing and preventing disease burden across the Nation. As biological sciences generate a deeper understanding of the working of organisms at the molecular and systems levels, opportunities open to advance our knowledge of the effects of environmental exposures—not just the clear and obvious effects, but also the subtle, complex ways human health is affected by the environment. Tackling scientific questions with this level of complexity requires an ongoing evaluation of our ideas and approaches, and an emphasis on integration across disciplines—from computational and molecular, to clinical and public health, and everything in between. Our discoveries translate into improvements in environmental regulation, public health, and clinical practice.

To improve our Nation's health, and to increase the benefits of our health care system, the use of medical interventions must go hand in hand with the adoption of behaviors aimed at disease prevention and wellness promotion. The goal of environmental health sciences is to remove human exposures to deleterious agents before disease processes and dysfunction begins. By advancing our understanding of the interactions of the environment with human health, and opening the door to new ways to prevent disease, NIEHS's investments serve to undergird a recovering economy and to support improvement of the health of our citizens, as well as our healthcare system. NIEHS budget request and research projects are also consistent with the President's multi-year commitment for cancer, autism, and nanotechnology.

NEUROLOGICAL DISORDERS AND THE ENVIRONMENT

There is continued concern that neurological disorders such as autism, attention deficit hyperactivity disorder (ADHD), and adult onset diseases such as Parkinson's and Alzheimer's may be rooted in early exposures to environmental toxicants. NIEHS supports basic research to determine the mechanisms and pathways by which toxicants may bring about neural damage to the developing brain. Some of the key neurotoxicants being studied are metals such as lead, mercury, and manganese; pesticides; tobacco smoke; and polychlorinated biphenyls and polybromated diphenyl ethers used to make insulating and fire retardant products.

With NIEHS support, the Children's Center at the University of California, Davis is conducting the first large-scale human population study of children with autism. These researchers are looking at a wide range of environmental exposures and their effects on early development in more than 1,000 California children. NIEHS researchers are also developing new and improved animal and cellular models for ADHD and autism—models that will help determine how neurotoxic substances may impact brain development and behavior, and may be useful in testing therapies.

ENVIRONMENTAL HEALTH AND SAFETY OF NANOMATERIALS

Engineered nanoscale materials display novel physical, chemical, and biological properties that contribute to new technologies useful for drug delivery systems, tissue engineering, biological and environmental sensor technology, and environmental remediation. By 2015, the global nanotechnology market is projected to exceed $15 billion. Nanotechnology, like all emerging technologies, should create innovation while minimizing risk of adverse health effects, and health effects of exposure should be assessed prior to extensive use. Safety assessment is challenging due to the diversity of materials used to synthesize nanoparticles, as well as the wide range of physical and chemical properties that emerge at the nanoscale. NIEHS and the National Toxicology Program (NTP), which is headquartered at NIEHS, support research on the impact of size and size-dependent properties of nanomaterials on biological response at the systemic, cellular, and molecular levels. This research has begun to demonstrate trends in the relationship of physical and chemical properties to biological response. NIEHS and NTP will continue to support research that increases the understanding of potential health impacts of these novel materials, as well as help to guide development of nano-enabled products to reduce adverse health impacts in our increasingly exposed population.

ENVIRONMENTAL DISRUPTORS OF ENDOCRINE SYSTEMS

Chemicals can mimic the hormones of our endocrine system and disrupt its functions, with potentially adverse effects on health and development. A consensus statement expressing concerns about the possible health effects of one such chemical, Bisphenol A (BPA), was issued by an expert panel as a result of a meeting organized by NIEHS in November 2006.

NTP also recently completed an evaluation of BPA. BPA was selected for evaluation because of the volume produced, widespread human exposure, extensive animal data on reproductive and developmental effects, and growing public concern. BPA is used in plastic water bottles and containers, in some medical tubing, and in the plastic coating inside of food cans, among other uses. Data from the Centers for Disease Control and Prevention showed BPA in 93 percent of 2,517 urine samples from people 6 years and older. The NTP evaluation graded various health concerns on a six-level scale: serious concern for adverse effects; concern; some concern; minimal concern; and negligible concern. NTP concluded there is "some concern" for effects on the development of the brain and behavior, and prostate gland development, in fetuses, infants, and children at current exposures, and "minimal concern" for effects on mammary gland and earlier age of female puberty in fetuses, infants and children at current levels of exposure. As a result of NTP's work, scientists at the Food and Drug Administration are reviewing their policies on BPA.

In separate NIEHS-supported studies in rats, BPA exposure induced changes in the mammary gland that were time and dose specific, so that, for example, high-dose exposure resulted in architectural modifications in the number of undifferentiated epithelial structures of the breast tissue. High-dose exposures induced changes in genes related to cell differentiation suggesting alterations in the normal development of the gland. These studies are part of the larger NIEHS-National Cancer Institute program of Breast Cancer and Environmental Research Centers; NIEHS expects that these and other research findings will shed light on the ways in which environmental exposures can influence the risk of breast cancer in women.

HEXAVALENT CHROMIUM AND HEALTH

Chromium compounds, such as hexavalent chromium, are widely used in electroplating, stainless steel production, leather tanning, textile manufacturing, and wood preservation. The United States is one of the world's leading producers of chromium compounds. Hexavalent chromium compounds have been shown to cause lung cancer in humans when inhaled, but it was not known whether these compounds could also cause cancer when ingested; hence they were nominated for NTP toxicity and carcinogenicity testing because of concerns over its presence in drinking water, its potential health effects, and the lack of adequate cancer studies on ingested hexavalent chromium.

NTP studies showed that sodium dichromate dehydrate, a compound containing hexavalent chromium, causes cancer in laboratory animals following oral ingestion. Male and female rats developed malignant tumors in the oral cavity. In mice, the studies showed dose-related increases in the number of benign and malignant tumors in the small intestine. This is the first and only lifetime study that clearly demonstrates the carcinogenicity of hexavalent chromium in rodents after oral exposure.

The results of these studies were closely monitored by many groups, including the affected industries and numerous national and international public health and regulatory agencies. The data will most certainly be used as the basis to develop State and Federal drinking water and soil cleanup standards, and will have significant public health impact on thousands of people exposed to hexavalent chromium in contaminated drinking water and soil.

CONCLUSION

These examples highlight important NIEHS and NTP research on the environmental connection to human disease and stand in for other vital research supported by the Institute. Research, such as the Sister Study, an epidemiological study following a cohort of 50,000 sisters of women diagnosed with breast cancer, promises to produce ground breaking information on the environment's role in the causation of breast cancer.

The field of environmental health sciences is beginning a new chapter of scientific progress, with new and better tools at our disposal, an expanding understanding of the human genome and its relationship with the environment, and young scientists coming into the field who are well-prepared and eager to apply these tools and knowledge to our current scientific challenges. I am honored, as Director of NIEHS and NTP, to facilitate the challenges and opportunities ahead to alleviate suffering and improve human health.

PREPARED STATEMENT OF DR. JEREMY M. BERG, DIRECTOR, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Mr. Chairman and members of the subcommittee: I am pleased to present the fiscal year 2010 President's budget request for the National Institute of General Medical Sciences (NIGMS). The fiscal year 2010 budget includes $2,023,677,000, which is $25,876,000 more than the fiscal year 2009 appropriation of $1,997,801,000.

Each year, NIGMS-supported scientists uncover new knowledge about fundamental life processes. While answering basic research questions, these scientists expand our awareness and understanding of how disease takes hold in the body. Institute grantees also develop important new tools and techniques that have research and medical applications. The payoffs from NIGMS research investments are impressive on many fronts. As just one example, 67 scientists have received Nobel Prizes in recognition of the scientific breakthroughs they made with NIGMS support.

GENETIC STUDIES GUIDE TREATMENTS

The future of medicine will center on precise diagnosis and personalized treatments. This is a departure from most of today's medical approaches, which are based on studies of populations and one-size-fits-all statistics derived from them. The ability to pre-emptively tailor healthcare to individuals offers huge potential for increasing the efficiency and effectiveness of efforts to preserve health over the course of a lifetime.

Americans are eager for information that will help them make intelligent, individualized choices about their health. Toward this end, in 2000 NIGMS partnered with a number of other National Institues of Health (NIH) components in launching an effort to determine how genes affect the way people respond to medicines, including antidepressants, chemotherapy agents, and drugs for asthma and heart disease. Since then, studies by this Pharmacogenetics Research Network (PGRN) have shown that genetic information can help predict how beta-blockers, breast cancer medications, and nicotine patches will work in a specific person. In early 2009, PGRN researchers merged data sets from around the world to demonstrate that information about certain genetic variations could aid doctors in determining the proper, personalized dose of warfarin, a blood-thinning drug taken by millions of Americans. This work set the stage for a prospective clinical trial that will test if using such genomic information will make it quicker and easier to get the right dose and furthermore, whether doing so could prevent serious treatment complications like heart attacks, strokes, and internal bleeding.

Other NIGMS-funded genetic studies have revealed surprising roles for RNA. Nobel laureates Andrew Fire and Craig Mello paved the way for this paradigm shift by showing that a process called RNA interference, or RNAi, silences the activity of targeted genes. RNAi is now being widely used both as a research tool and for the development of products that could combat diseases like cancer and HIV. In 2008, other NIGMS-supported scientists won the prestigious Lasker Award for their

groundbreaking discovery of microRNAs, short RNA molecules that regulate gene function using some of the same mechanisms central to RNAi. Our rapidly expanding understanding of RNA's many roles is already providing novel medical insights, such as the linkage of abnormal microRNA levels to cancer and other diseases.

PHYSICAL SCIENCES SHINE LIGHT ON BIOLOGY

The intersections between fields of science—such as those between the physical sciences of physics, chemistry, mathematics, and computer sciences and the biomedical and behavioral sciences—often yield particularly fruitful and high-impact lines of investigation. One timely example is the NIGMS-supported computational modeling tools being used to predict the spread of emerging infectious diseases and the results of possible interventions. These field-spanning approaches provide important insights to help policymakers and public health officials respond to outbreaks, including H1N1 flu.

Further evidence of how basic physical science can greatly contribute to biomedical research is found in nuclear magnetic resonance (NMR). This technique, developed by physicists in the 1930s, underlies the well-known medical procedure of magnetic resonance imaging. But in the laboratory, NMR is the basis of some of the most powerful analytical methods in chemistry and biochemistry. In 2008, NIGMS-funded researchers used NMR to identify a contaminant in several batches of another widely used blood-thinning medicine, heparin. The scientists determined the chemical structure of the contaminant, which was only subtly different from heparin and therefore difficult to find by other methods, and showed how the contaminant could cause severe reactions and even death in humans. As a result of this work, NMR may now be used to screen additional drug preparations for contaminants that are difficult or impossible to detect by other means.

A physics-based technique called X-ray crystallography is also key to understanding molecules that are central to health and disease. Using this approach along with NMR, scientists funded through a coordinated NIGMS effort called the Protein Structure Initiative (PSI), have produced a wealth of information about the shapes of proteins, which are essential to their functioning. Following successful pilot and production phases that included the development of critical tools and techniques, the Institute is now focusing the PSI on structures with specific biological roles and expanding its reach throughout the scientific community. This new direction, called PSI:Biology, will emphasize partnerships between biologists and high-throughput structure determination centers to address important biomedical problems and provide information that will aid the development of new medicines.

Among the advances from chemistry studies are powerful imaging techniques that allow scientists to visualize life processes in unprecedented detail. The discovery and development of green fluorescent protein (GFP) is a case in point. GFP was first purified from jellyfish in 1962, and before long, NIGMS-funded American researchers were finding ways to use this new tool to monitor activities in living cells and organisms. These scientists, who won the 2008 Nobel Prize in chemistry for their insights, put the GFP gene into a variety of organisms, including bacteria and worms. Today, GFP is an essential part of the fabric of biological research and is used, for example, as a key component of powerful drug development tools.

FINDING AND FUNDING INNOVATION

To keep knowledge streaming from the Nation's scientific laboratories, we must be agile in responding to the changing needs of researchers, both individuals and teams. The Institute has been a pioneer in novel funding programs that address the needs of the scientific community and encourage innovation. One good example is Konrad Hochedlinger, who received an NIH Director's New Innovator Award in 2007. This program, which NIGMS developed and administers, jump-starts the careers of unusually creative early stage investigators. Since groundbreaking work in 2007 in which other NIGMS-funded scientists reprogrammed ordinary skin cells to become induced pluripotent stem cells (iPS) this area of inquiry has exploded. Dr. Hochedlinger's project aims to unravel the many details of how reprogramming works. He is currently working on creating "reprogrammable mice" in which every cell can become an iPS cell capable of morphing into any cell type.

Another New Innovator is explaining basic behavioral principles using animal models. Karin Pfennig is studying how different species of toads choose a mate, a decision that has costs and benefits and involves trade-offs. Understanding the fundamental drivers of such "context-specific" behavior may help us treat behavioral disorders in people and address behavioral aspects of disease transmission and spread.

Dr. Pfennig has contributed to the research enterprise in another important way. As part of its commitment to training the next generation of scientists and increasing the diversity of the scientific workforce, NIGMS developed the Institutional Research and Academic Career Development Award (IRACDA). This program gives postdoctoral scientists mentored teaching experiences at minority-serving institutions. Through IRACDA, Dr. Pfennig pursued her own cutting-edge research at the University of North Carolina, Chapel Hill, while also teaching at a historically Black college, North Carolina Central University. Dr. Pfennig, who grew up in a single-parent household with very limited resources, attributes her desire to "give back" to her own great teachers and mentors who challenged her to pursue her ambition to become a scientist. Programs like IRACDA pay lasting dividends on many levels, providing role models for students, preparing future teachers, and promoting partnerships between institutions.

INVESTING TODAY FOR AMERICAN PROSPERITY

In addition to building a solid foundation of knowledge for medical advances, basic biomedical and behavioral research yields tangible economic benefits. NIGMS grants support the salaries and laboratories of thousands of researchers throughout the United States. And NIGMS-funded advances have played a significant role in the development of the multi-billion-dollar biotechnology industry, which is now its own engine of discovery as well as a critical partner to the pharmaceutical industry.

I want to close by affirming the Institute's deep appreciation for the extraordinary opportunities provided by the American Recovery and Reinvestment Act of 2009. In addition to its impact on stimulating the Nation's economy, this legislation will enable scientists to uncover new knowledge that will lead to better health for everyone. We intend to use these funds to support highly meritorious research that could not be funded with our regular appropriations and to further accelerate the tempo of science through targeted supplements to existing grants. NIGMS is also addressing research projects which are consistent with the President's multi-year commitment for cancer and autism. We are also eager to fund creative studies sparked by the new NIH Challenge and Grand Opportunities grant programs, which are designed to focus on health and science problems where significant progress can be expected in 2 years.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the subcommittee may have.

PREPARED STATEMENT OF DR. THOMAS R. INSEL, DIRECTOR, NATIONAL INSTITUTE OF MENTAL HEALTH

Mr. Chairman, and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Mental Health (NIMH) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $1,474,676,00, which is $24,185,000 more than the fiscal year 2009 appropriation of $1,450,491,000.

PUBLIC HEALTH BURDEN OF MENTAL ILLNESS

According to the most recent estimates, roughly 12.5 million American adults reported mental illness symptoms so severe as to cause them significant disability in the past year.[1] [2] According to the World Health Organization, mental disorders are the leading cause of medical disability in the United States and Canada for people under age 45. In contrast to many other chronic medical conditions, mental disorders typically begin at an early age, usually before the age of 30. Indeed, mental disorders, such as schizophrenia, depression, and bipolar disorder, are increasingly recognized as the chronic medical illnesses of young people. These illnesses also shorten people's lives. Americans with serious mental illness die, on average, 25 years earlier than the general population.[3]

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[1] Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM–IV disorders in the National Comorbidity Survey Replication (NCS–R). *Archives of General Psychiatry*, 2005 Jun;62(6):617–27.

[2] U.S. Census Bureau. *Population Estimates by Demographic Characteristics. Table 2: Annual Estimates of the Population by Selected Age Groups and Sex for the United States: April 1, 2000 to July 1, 2004* (NC–EST2004–02) Source: Population Division, U.S. Census Bureau Release Date: June 9, 2005. http://www.census.gov/popest/national/asrh/

[3] Parks J, Svendsen D, Singer P, Foti ME (Eds.). *Morbidity and mortality among people with serious mental illness*. Alexandria, VA: Medical Director's Council, National Association of State

Continued

The annual economic costs of mental illness in the United States are enormous. The direct costs of mental health treatment represent 6.2 percent of all healthcare spending,[4] which, according to the Centers for Medicare and Medicaid Services, totaled 15.8 percent of the gross domestic product in 2003. Indirect costs associated with mental illness, which include all nontreatment-related costs such as lost earnings, Social Security disability payments, homelessness, and incarceration, account for even greater expenses than the costs of direct mental healthcare. A recent study found that serious mental illnesses cost the United States at least $193 billion annually in lost earnings alone.[5] A conservative estimate places the total direct and indirect annual costs of mental illness at well over $300 billion.[6]

MENTAL DISORDERS ARE CHRONIC BRAIN DISORDERS

NIMH's mission is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. These illnesses can now be studied as brain disorders, as they are becoming more accessible to medical science by using the tools of modern neuroscience. These disorders frequently begin in childhood and are chronic, affecting people of all races and ethnicities, in both rural and urban settings. To prevent a lifetime of disability for millions of Americans, NIMH research is directed toward identifying the biological basis of mental disorders, examining the psychological and social aspects that contribute to the disorders, and pinpointing targets for improved prevention, diagnosis, and treatment.

MENTAL HEALTHCARE IN THE FUTURE

In the future, the practice of medicine will be increasingly predictive, pre-emptive, personalized, and participatory. Genetics and clinical neuroscience will make this possible for mental illnesses. Clinical neuroscience seeks to discover fundamental knowledge about the brain and behavior and to use this knowledge to develop better tools for prevention, diagnosis, and treatment. For instance, biomarkers can detect risk to permit prevention, neuroimaging may facilitate diagnosis, and the discovery of new molecular targets should yield novel treatments. The study of pathophysiology is fundamental for NIMH's mission, which is to use science to transform care: not merely to reduce symptoms among persons with mental illness, but to promote recovery among this population and ultimately to discover preemptive interventions that can prevent psychosis, disability, and suicide.

In pursuit of this mission, NIMH is in the process of implementing its new Strategic Plan, which details the scientific priorities that will direct and accelerate mental health research in the years to come. The American Recovery and Reinvestment Act of 2009 (the Recovery Act) directs part of the Nation's stimulus funding to support job creation and retention in the field of biomedical research. These supplemental funds present an exciting opportunity for NIMH, allowing us to jumpstart the groundbreaking science outlined in the Strategic Plan, as well as the strategic plans of the NIH Office of AIDS Research and the Interagency Autism Coordinating Committee (IACC). This commitment will expand our knowledge about the underlying biology of mental disorders and accelerate the development of improved diagnostic measures and treatments. The fiscal year 2010 budget continues support for the IACC. NIH will receive $1 million from the Office of the Secretary to support the Committee.

Mental healthcare in the future will be based on the ability to predict those most at risk, prevent the onset of disorder, and, in cases where prevention is not possible, develop treatments tailored to the individual. This requires collaboration among the diversity of people affected, including mental healthcare providers, researchers, and people with mental illness and their families. An example of NIMH research taking

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Mental Health Directors (NASMHPD). October 2006. http://www.nasmhpd.org/general__files/publications/med__directors__pubs/Technical%20Report%20on%20Morbidity%20and%20Mortality%20-%20Final%2011–06.pdf

[4] Mark TL, Levit KR, Coffey RM, McKusick DR, Harwood HJ, King EC, Bouchery E, Genuardi JS, Vandivort-Warren R, Buck JA, Ryan K. *National Expenditures for Mental Health Services and Substance Abuse Treatment, 1993–2003*. SAMHSA Publication No. SMA 07–4227. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2007. http://www.samhsa.gov/spendingestimates/SAMHSAFINAL9303.pdf.

[5] Kessler, RC, Heeringa S, Lakoma MD, Petukhova M, Rupp AE, Schoenbaum M, Wang PS, Zaslavsky AM. The individual-level and societal-level effects of mental disorders on earnings in the United States: Results from the National Comorbidity Survey Replication. *Am J Psychiatry*. 2008 Jun; 165(6):703–11.

[6] Insel TR. Assessing the economic cost of serious mental illness. *Am J Psychiatry*. 2008 Jun; 165(6):663–5.

this approach is our recent partnership with the U.S. Army to reduce suicide among soldiers. The high rates of mental health and behavioral adjustment problems among recent U.S. military combat veterans and the increasing rates of suicide among Army soldiers are of growing concern. To address this issue, NIMH and the U.S. Army are collaborating on a $50 million research project, which will be the largest single study NIMH has undertaken on the subject of suicide. The project seeks to strengthen the Army's efforts to reduce suicide among soldiers by identifying the risk and protective factors associated with suicidal thinking and behavior. While targeted for the Army, the study's findings will also inform our understanding of suicide in the other Armed Forces as well as the overall population, leading to more effective prevention and treatment for servicemembers and civilians alike.

While we have long known that mental disorders are brain disorders, recent research has begun to reconceptualize these illnesses as disorders of brain development. Between infancy and adulthood dramatic changes are taking place in the brain, not only in size, but also in structure and function. Understanding these changes and how these trajectories can go off course provides unprecedented promise for the prediction and prevention of mental disorders, as well as opportunities to harness this knowledge to improve treatments for individuals who go on to develop a disorder, either in childhood or in early adulthood. As an example, research on brain development in children with attention-deficit/hyperactivity disorder (ADHD) from the NIMH Intramural program recently reported a striking delay in cortical maturation. Between ages 5 and 15, the maturation of the prefrontal cortex was found to be delayed by roughly 3 years in children with ADHD compared to age-matched children without the disorder. Current studies are now exploring the effects of treatment on the rate of cortical maturation.

The prototype neurodevelopmental disorder for NIMH is autism. Matching the increasing public health urgency of autism, NIMH research over the past year has yielded important discoveries on the pathophysiology of autism spectrum disorders (ASD). Research has shown that different cases of ASD could potentially be traceable to any of 50 or more variations in the genome, alone or in combination, suggesting that ASD may be the final common path for many different genetic abnormalities. Most of the genes implicated are critical for brain development. For example, independent teams of researchers have linked inherited variations in a gene on Chromosome 7, called CNTNAP2, with ASD. CNTNAP2 is part of a family of genes that make proteins that play a key role in building the machinery by which brain cells communicate. One variation of this gene was found to influence the age at which children with ASD say their first word. Another variation was identified that increases the risk for ASD, but mainly when it is inherited from mothers. These studies provide evidence that CNTNAP2, when disrupted, may represent one path to the development of ASD. In addition to breakthroughs in the genetics of autism, recent research has provided new tools for diagnosing autism as early as the first birthday. Early diagnosis is critical because early intervention is associated with the best outcomes.

In order to build upon these research advances, NIMH will be using Recovery Act funding as an opportunity to fuel further research on ASD, including its underlying biology, methods for earlier and more effective diagnosis, and improvements in treatment. The new IACC Strategic Plan for ASD Research provides the scientific goals and benchmarks for this endeavor (www.iacc.hhs.gov). NIMH, in collaboration with other NIH Institutes, has issued a series of funding opportunity announcements (FOA) to address the heterogeneity of ASD. This will be the largest single funding opportunity for ASD research in NIH's history. NIMH may contribute as much as $30 million of the total $60 million of Recovery Act funds that NIH has set aside for this effort (actual expenditures will depend on the proposals received). These FOAs encourage applications for 2-year projects that address ASD measurement, identification of biomarkers and biological signatures, immune and central nervous systems interactions, genetics/genomics, environmental risk factors, and ASD intervention and treatment. Additionally, we will be supporting autism research with Recovery Act funding through NIH's new Challenge Grants in Health and Science Program. This program encourages applications on a diverse range of research topics, such as improving access to services by individuals with ASD and their families and expanding NIH's National Database for Autism Research in order to accelerate the availability of new data for the ASD research community. Finally, NIMH intends to continue to build its investment in autism research via its base budget, which supports a new intramural program for autism research, Autism Centers of Excellence, and a broad range of individual grants for research and training related to ASD.

Understanding the pathophysiology underlying mental disorders will not only lead to the improved prevention, diagnosis, and treatment of the disorders themselves,

but will also help to clarify the relationships that exist between mental disorders and other physical health problems, such as cancer. People with mental disorders smoke cigarettes at twice the rate of those without such a disorder, and they consume 44 percent of all cigarettes smoked in the United States.[7] NIMH research is not only addressing this major public health problem through behavioral studies on smoking cessation techniques in these populations, but is also seeking to understand the underlying causes of smoking behavior. Several studies are examining the link between cognitive function, which is often disrupted in severe mental illness, and its improvement through nicotine use. By gaining better insight into how nicotine influences neural mechanisms, NIMH researchers are hoping to discover new ways of improving cognitive function among people with mental illness, ultimately reducing the severe health consequences associated with tobacco use.

In summary, we are well positioned to fulfill the promise of predictive, preemptive, personalized, and participatory medicine in the future. By using the best tools, funding the best science, listening to our partners, and engaging our communities, we continue to make progress toward our goal of transforming the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

PREPARED STATEMENT OF DR. STORY C. LANDIS, DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $1,612,745,000, which is $19,401,000 more than the fiscal year 2009 appropriation of $1,593,344,000.

The important and challenging mission of NINDS is to reduce the burden of neurological disorders through research. Hundreds of disorders of the brain, spinal cord, and the nerves of the body affect people of all ages. Collectively, they cause an enormous burden in lost life, disability, and suffering, and cost billions of dollars each year in medical expenses and reduced productivity. The causes of nervous system disorders are diverse; among them are physical forces of traumatic brain injury, slow degeneration of nerve cells in Parkinson's and Alzheimer's disease, gene mutations in brain tumors and inherited diseases, blood vessel block or bleeding in stroke, and toxic effects of treatments for cancer, HIV/AIDS, and other diseases. Compounding the challenge, the brain and spinal cord are intricate in structure, difficult to access, sensitive to intervention, and do not readily repair themselves following damage.

PLANNING FOR THE FUTURE

Over the last 2 years, NINDS has engaged the scientific community and the public in strategic planning to meet these challenges. Planning took a "blue sky" look at the future, but also gave outside experts unprecedented access to data about NINDS programs to inform recommendations of practical steps to better carry out our mission. Even as we finalize the strategic plan and seek further public input, we are implementing recommendations. One major lesson from planning is the importance of program evaluation; based on the results we are reallocating resources to maximize public health impact. Perhaps the most important message for today, however, is not at the level of program details, but about where we stand with respect to the NINDS mission-treatments for neurological disorders are still far from adequate, but research is yielding remarkable progress, and the prospects for the future are very encouraging.

NINDS's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism.

STROKE

Stroke, the "S" in NINDS, shows how far we have come and how far we have to go. Stroke remains the third leading cause of death in the United States and a major cause of long-term disability. However, American Heart Association statistics show that the age-adjusted stroke death rate decreased by 29.7 percent from 1995 to 2005, and actual stroke deaths declined by 13.5 percent, resulting in thousands of lives saved. Many NIH research studies contributed to the decline by predicting

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[7] Ziedonis D., et al. Tobacco Use and Cessation in Psychiatric Disorders: National Institute of Mental Health Report. *Nicotine Tob Res*, 2008;10: 1–25.

who is at risk for stroke, who will do best on which drug, and whether surgery to clean a carotid artery or repair an aneurysm is worth the risk for a particular patient. Research on stroke prevention is continuing apace, including research on the geographic and racial disparities.

About a decade ago, a NINDS clinical trial demonstrated that appropriate use of the clot buster tPA can restore blood flow to the brain and significantly improve outcome from stroke. New clinical trials are building on this first successful emergency treatment by testing whether ultrasound improves tPA's effectiveness to break up clots in large brain arteries and whether direct injection of tPA into a blocked brain artery or clot retrieval devices may help some patients. Despite its proven benefit, too few people now receive tPA, which must be administered after specialist assessment and within a few hours of a stroke. A trial this year showed that telemedicine can expand access to emergency stroke treatment to areas of the country without specialized stroke centers. A second trial is assessing whether emergency personnel in the field can rapidly deliver a therapy to protect the brain prior to reaching a hospital. Beyond prevention and emergency treatment, a major challenge for stroke, as for traumatic brain injury, is promoting recovery after brain damage has occurred. Rehabilitation that harnesses the brain's "plasticity" is showing promise in people, and trials are assessing the most effective strategies, but there is still a long way to go.

GENES AND BRAIN DISEASES

Although there are hundreds of neurological disorders, common themes unify research across diseases. One lesson of planning is the importance of engaging the insight and ingenuity of researchers throughout the United States to recognize shared disease mechanisms and common therapeutic strategies. Research on genes is one unifying theme that spans many areas of basic and clinical science.

A first wave of progress identified single gene defects that cause more than 200 neurological disorders, and continues with new findings in inherited types of ALS and other diseases. Often, the most immediate benefit of gene findings is genetic tests, which can spare families expensive and frustrating diagnostic odysseys to find out what is wrong with their child. Even when a single gene defect is identified, major obstacles confront therapy to correct the defect, especially in the brain, but there is progress; this year, for example, a preliminary clinical trial established the feasibility of gene transfer to treat Batten disease. Genes can also provide the first foothold on understanding causes and developing drug treatments, leading to rational therapy development programs, as NINDS has underway for muscular dystrophy, spinal muscular atrophy, and other disorders. Although most brain tumors are not inherited, acquired gene defects drive tumor formation. Observing which genes are affected in glioblastoma and other brain tumors is suggesting which tumors respond to which cancer drugs and providing clues to developing more effective treatment.

Recently, scientists have begun to crack the more complex ways that variations in multiple genes together contribute to common neurological disorders and shape individual differences in therapy response. Gene tests show promise for establishing the appropriate dose of the drug warfarin, which is commonly used to prevent stroke in people with certain risk factors. Warfarin now requires frequent blood tests to find the safe and effective dose because of variability among people, and people are at risk until the dose is set. Genome-Wide Association Studies (GWAS) are one method that has associated genes with multiple sclerosis, Parkinson's disease, stroke, and other common disorders. For example, understanding autism is an NIH-wide priority, and

GWAS recently implicated molecules that have been studied in the development of connections among nerve cells, linking a dynamic area of basic research to this disease.

TRANSLATING SCIENTIFIC INSIGHTS TO THERAPIES

NINDS basic and clinical research yield understanding of disease and clinical tools that are essential for therapy development in the private sector. The Institute has also long pursued translational opportunities that are not likely to be targeted by others, whether because bold therapeutic strategies present uncertainty and long development horizons that are not tolerable to investors, rare diseases represent a small market, or developments in surgery and interventions using existing drugs may not recapture investments. The NINDS Intramural program developed the first successful enzyme therapy for inherited disease. Among applied NINDS extramural programs, the Anticonvulsant Screening Program has catalyzed the development of several epilepsy drugs now on the market, and the Neural Prosthesis Program successfully pioneered devices to restore lost nervous system functions. In 2003, NINDS

moved from selective translational research in a few areas, to a broad effort to capitalize on opportunities across all neurological disorders by initiating the Cooperative Program in Translational Research. This program supports academic and small business investigator-initiated preclinical therapy development, using milestone driven funding and peer review expertise and criteria tailored to therapy development. Therapies from this program have received investigational approval from the FDA and are moving to clinical trials. Based on the advice of strategic planning advisory panels, which included industry experts, NINDS has created an Office of Translational Research and recruited a leader who has extensive drug development expertise. The new office will coordinate and focus NINDS applied programs more effectively on therapy development, without reducing NINDS commitment to basic and clinical research that is the foundation for progress. As new opportunities for therapy development emerge, we cannot let them languish in the "valley of death" between the idea and the success.

Progress against two gene disorders that cause nervous system tumors illustrates how basic understanding of disease can drive research toward treatment. In people who have neurofibromatosis type 1, tumors grow within nerves and can cause disabling symptoms by compressing nerve, spinal cord, and other organs. Several years ago NIH-funded investigators discovered gene mutations that cause the disease and developed animal models that mimic the human disorder. After years of work, researchers discovered how the mutant gene causes cells associated with nerves to develop tumors, and then recruit other cell types and blood vessels to the tumor. Once researchers understood the molecular steps, they recognized that the cancer drug Gleevec acts on the same molecules. They are now testing the drug in people who have neurofibromatosis.

Tuberous sclerosis complex is another disorder in which tumors, called tubers, can grow in nearly any tissue, including the brain. Many people with this disease also develop epilepsy or autism. Again, finding genes led to understanding of the molecular steps in disease, and scientists recognized that an available drug, rapamycin, which is used to prevent organ transplant rejection, affects a key molecule in the disease process. Studies in mice that mimic the human disorder were especially encouraging because the results suggest that the disease can be reversed in adults, countering pessimism that the disease produced irreversible affects on brain development. Researchers are exploring whether rapamycin or similar drugs are safe for long-term use, and may also be of benefit for epilepsy or autism from other causes.

THE RESEARCH WORKFORCE

As science progresses, we recognize themes that bring together research on disparate diseases, whether shared disease mechanisms, as in neurodegeneration, therapeutic approaches, as stem cells, or program needs, as translational research. The American Recovery and Reinvestment Act reminds us of another common theme—research is labor intensive. Progress depends on the men and women who do research and their commitment to research that may take decades. To maintain the vigor of NIH and private research, NINDS is committed to making research an attractive and sustainable career for young people who are innovative, intelligent, dedicated, and diverse.

PREPARED STATEMENT OF DR. PATRICIA A. GRADY, DIRECTOR, NATIONAL INSTITUTE OF NURSING RESEARCH

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Institute of Nursing Research (NINR) of the National Institutes of Health (NIH). The fiscal year 2010 budget request includes $143,749,000, which is $1,870,000 more than the fiscal year 2009 appropriation of $141,879,000.

NINR's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism.

INTRODUCTION

NINR supports clinical and basic research to build the scientific foundation for clinical practice, prevent disease and disability, manage and eliminate symptoms caused by illness, and enhance end-of-life and palliative care. The breadth and depth of NINR's research portfolio is ideally suited to explore some of the most important challenges affecting the health of the American people. An aging population, an increasing incidence of chronic illness, a shortage in the health workforce, and rapidly escalating costs necessitate profound changes in the ways in which we ap-

proach healthcare. These challenges require us to develop new strategies for treating, managing, and preventing illness that are person-centered rather than disease-centered, that focus on pre-empting the development of chronic illness rather than treating it, and that feature the person as an active participant in managing his or her own healthcare. The research supported by NINR can significantly contribute to the evidence base for many of the changes that will occur in healthcare in the coming years and decades. NINR advances science to address current and future challenges through its research programs in health promotion and disease prevention; self-management, symptom management, and caregiving; and end-of-life and palliative care. In addition, NINR maintains a strong commitment to the elimination of health disparities faced by at-risk and underserved populations through continued work to develop culturally appropriate, evidence-based interventions. NINR also trains the next generation of scientists to ensure the development of the innovative research and faculty workforce of the future. The research goals in NINR's strategic plan, changing practice, changing lives, emphasize the areas of public health that demonstrate the greatest needs and in which NINR can have the greatest impact.

Let me now describe our research programs and highlight some of our recent accomplishments.

NINR RESEARCH PROGRAMS

Health Promotion and Disease Prevention

Healthcare professionals and policy leaders have stressed the importance of preventive care to the health of all Americans. NINR supports research to discover new ways to prevent disease and achieve long-term, positive health outcomes in individuals across the lifespan. NINR-supported scientists explore strategies to understand and promote behavioral changes in individuals, evaluate health risks in diverse communities, and assess issues of patient safety. In recent years, successful efforts in the areas of health promotion and disease prevention research have increasingly involved community members in the design and conduct of the study.

NINR research has an impact on clinical practice. In one example, researchers designed, implemented and evaluated a program to address the health burden and costs associated with premature birth, a condition affecting more than 500,000 infants in the United States every year. The Creating Opportunities for Parent Empowerment program (COPE), for parents of premature infants, is an educational-behavioral intervention program that begins 2 to 4 days after admission to a neonatal intensive care unit (NICU) and teaches parents how to care for their premature infant. The researchers found that COPE implementation reduced the length of stay in the NICU by 4 days, for an estimated healthcare cost savings of at least $4,800 per infant. Thus, in addition to improving parent and child outcomes, routine implementation of COPE in NICU's across the United States could possibly save the healthcare system more than $2 billion per year. The results of this study have sparked interest among hospitals and insurers nationwide.

NINR-supported researchers are developing more programs to promote healthy behaviors and prevent disease, including: an outreach intervention designed to reduce HIV-risk among adolescent girls receiving services through community-based health centers; a parent training program designed to promote positive parenting and mental health among low-income ethnic minority families with young children; and a lifestyle-modification program for prehypertensive, middle-aged rural women.

SELF-MANAGEMENT, SYMPTOM MANAGEMENT, AND CAREGIVING

Given the increasing numbers of people living with chronic illness, whether children with diabetes or elders with heart disease, NINR is developing new approaches to help individuals manage their own health conditions, to decrease the effects of adverse symptoms, and to reduce the burden on caregivers. NINR is improving the quality of life of individuals with chronic illness and their families by supporting research related to self-management, symptom management, and caregiving.

Our self-management research explores strategies that help individuals to participate in their own health practices. In one recent example, community "Lay Health Educators" were trained to deliver a health promotion and asthma management program to children in elementary schools from rural towns and unincorporated communities. Children receiving this program demonstrated significant improvements in asthma knowledge, self-management scores, and use of metered dose inhalers. Results from this study suggest that using Lay Health Educators for delivery of an in-school education program may be an effective means for improving children's skills in asthma self-management, especially in hard-to-reach communities.

Our symptom management research focuses on the biological and behavioral aspects of symptoms such as pain and fatigue, with the goal of improving patient health and quality of life. A recent symptom management study aimed to define patient-determined success for treatment of chronic spine pain in four areas: pain, fatigue, emotional distress, and interference with daily activities. This study found that the patients for whom pain was reduced experienced significantly less fatigue, emotional distress, and interference with daily activities. The findings confirm that successful treatment for chronic pain is not viewed by patients exclusively in terms of pain reduction, but also involves a number of additional quality of life factors.

Research Capacity Development

The increasing demand for nurse clinicians, faculty, and scientists, and the inadequate supply of new nurses to meet that need, continue to burden America's health system. NINR builds research capacity and fosters interdisciplinary training for the next generation of scientists in basic, translational, and clinical research through individual and institutional training and career development awards. NINR training strategies focus on the development of nurse scientists and earlier entry into research careers with special consideration given to underrepresented and disadvantaged populations. In addition, innovative training programs at the NIH, such as the NINR Summer Genetics Institute, the NINR Graduate Partnerships Program, and the new BNC fellowship (a joint venture between NINR, the NIH Clinical Center, and the Bravewell Collaborative), all serve to increase the knowledge and experience base of new scientists, and assist them in their transition to long-term research careers.

End-of-life

Faced with a complexity of life-limiting and eventual terminal conditions—whether cancer, heart disease, stroke, or neurodegenerative disorders—the challenges experienced by patients and their families as life draws to a close have refocused attention to the end of life and necessitated a better understanding of the dying process, the associated decisions about treatment, and the quality of care patients receive. Focusing on these topics, NINR end-of-life research seeks through science to improve the understanding of the mechanisms underlying palliation, including pain, fatigue, depression, and related symptoms; enhances communication and decision-making processes between patients and family members; and develops effective strategies to optimize care across diverse settings, populations, and cultural contexts.

One recent study explored the relationship between diagnosis and advance directives. As part of a longitudinal study, patients with an expected 2-year survival of less than 50 percent who had either cancer or amyotrophic lateral sclerosis (ALS) were interviewed with the goal of determining whether and how end-of-life discussions differed between clinicians and patients. Results showed that cancer patients were less likely than ALS patients to have had advanced care planning discussions. Although these results may reflect perceptions that ALS has a more predictable disease trajectory, that advanced cancer has a greater number of treatment options, or the presence of differing views about hope, this study highlighted that cancer patients may be less than adequately prepared for end-of-life decisionmaking.

Another recent study examined the life support withdrawal process for patients who died in the intensive care unit (ICU) or within 24 hours of discharge from the ICU, and surveyed family members on their perceptions of the care provided. The researchers discovered that for family members of patients who had an ICU stay of 8 days or more, families were more satisfied with care received when withdrawal of life support occurred in a staggered progression. The outcome of this study indicates that clinicians need to work with the family throughout the patient's ICU stay to provide them with accurate information on which to base decisions, and prepare them emotionally for the possible loss of their loved one.

NINR AND THE AMERICAN RECOVERY AND REINVESTMENT ACT

Funding for scientific research received through the American Recovery and Reinvestment Act of 2009 (ARRA) has provided NINR with an enormous opportunity, not only to assist with the Nation's economic recovery by creating and retaining jobs and enhancing infrastructure, but to advance biomedical and behavioral research in areas of critical importance to the NINR mission. NINR is using the funds from ARRA to support additional research projects, to accelerate ongoing research through supplements to current grants, and to create opportunities for introducing prospective scientists to a research career. The additional science supported by NINR through ARRA will, in the long-term, contribute to improving the health of

the Nation through enhanced prevention and management of chronic illness and disease.

Thank you, Mr. Chairman. I will be happy to answer any questions that the subcommittee might have.

PREPARED STATEMENT OF DR. DONALD A.B. LINDBERG, DIRECTOR, NATIONAL LIBRARY OF MEDICINE

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the National Library of Medicine (NLM) of the National Institutes of Health (NIH). The fiscal year 2010 budget includes $334,347,000, which is $3,576,000 more than the comparable fiscal year 2009 appropriation of $330,771,000.

NLM, the world's largest biomedical library and the developer of electronic information services, delivers trillions of bytes of data to millions of users daily. Every day 3.5 terabytes of data are downloaded to users. By making research results—from DNA sequences to clinical trials data to published scientific articles and consumer health information—readily available, the Library magnifies the positive impact of the NIH's investment in the creation of new knowledge. By organizing increasing amounts and types of biomedical and health information, the NLM fuels new research discoveries, informs patient care decisions, helps people exert control over their health and healthcare, and AIDS disaster preparedness and response.

The NLM is a key enabler for important congressional, NIH, and Department of Health and Human Services (HHS) initiatives. NLM's budget request and its research projects are consistent with the President's multi-year commitment for cancer and autism. Current priorities include: increasing the transparency of clinical trials in ClinicalTrials.gov; enhancing public access to NIH-funded peer-reviewed manuscripts in the PubMed Central archive; making results of Genome-Wide Association Studies (GWAS) available in dbGaP to improve the understanding of genetic and environmental factors underlying human disease; supporting and distributing standard terminologies for electronic health records and clinical research data, including genetic tests, within NLM's Unified Medical Language System; conducting biomedical informatics research on health applications of information technology; and developing specialized information resources for use in emergency and disaster response.

To be useful, NLM's information services must be known and readily accessible. The Library's outreach program relies heavily on the 5,800-member National Network of Libraries of Medicine (NN/LM) and on exhibitions, events, and varied media to bring the message about NLM's free, high-quality health information resources to communities across the Nation. The NN/LM comprises academic health sciences libraries, hospital libraries, public libraries, and community-based organizations. They form an efficient way to make the published output of biomedicine easily accessible by scientists, health professionals, and the public and to develop partnerships with community organizations and underserved populations.

SCIENTIFIC INFORMATION RESOURCES

The NLM's National Center for Biotechnology Information (NCBI) meets the challenge of collecting, organizing, storing, analyzing, and disseminating scientific data by designing, developing, and distributing the tools, databases and technologies that are enabling the genetic discoveries of the 21st century. Celebrating 20 years since its enactment, the Center is at the hub of international interchange of molecular biology and genomic information, with Web sites accessed several million times a day.

In addition to the widely known GenBank and PubMed/MEDLINE databases, the NCBI provides a wide array of genomic resources and is a valued collaborator throughout the NIH. The recent discovery of a novel H1N1 influenza virus highlights the value of the specialized virus resource that NCBI developed with the National Institute of Allergy and Infectious Diseases. It links vaccine researchers to genomic data about the influenza virus. The PubChem repository fills a critical need in the Molecular Libraries Roadmap Initiative, with information on more than 40 million "small molecules" that are crucial in drug development. The dbGaP database, which links genotype data with phenotype information from clinical research studies to support identification of genetic factors that influence health, is the public repository for the trans-NIH GWAS project. NIH's mandatory Public Access Policy ensures scientific articles written by NIH-funded authors are deposited in PubMed Central and linked to other scientific information.

The Lister Hill National Center for Biomedical Communications leads research to create and improve biomedical communications systems, technologies, and networks. The Center recently completed a major expansion of ClinicalTrials.gov, in response to the congressional mandate. The system now maintains a registry of clinical trials involving FDA-regulated drugs, biologics, and devices and starting last September, began collecting summary results of trials of FDA-approved products. ClinicalTrials.gov currently contains data on more than 70,000 trials in 166 countries and is searched by more than 500,000 people every month.

The NLM's two research centers collaborate on improving standards for genetic and genomic testing. The NCBI provides a database of reference values to assist in quality control of genomic tests. The Lister Hill Center is helping to expand the Logical Observation Identifiers Names Codes standard to cover genetic and newborn screening tests already in routine clinical and public health use.

Electronic health records with advanced decision-support capabilities—and connections to relevant health information—will be essential to achieving personalized medicine and will also help people manage their own health. NLM supported much of the seminal research work on electronic records, clinical decision support and health information exchange. NLM is the HHS coordinating body for clinical terminology standards and supports development and dissemination of key standards for U.S. health information exchange. The Lister Hill Center is actively engaged in research on next generation electronic health records to facilitate patient-centered care, clinical research, and public health. This work has already resulted in tools that are helping system developers, including some at the Centers for Medicare and Medicaid Services, to incorporate the use of standards into health information systems.

INFORMATION SERVICES FOR THE PUBLIC

In addition to providing researchers and health care providers with access to scientific information, the NLM also serves the public—from elementary school children to senior citizens. The Library's main consumer health portal is MedlinePlus, available in both English and Spanish. In fiscal year 2008, there were more than 750 million MedlinePlus pages viewed by more than 132 million unique visitors from 229 countries. In addition to more than 725 "health topics," MedlinePlus has interactive tutorials for persons with low literacy, medical dictionaries, a medical encyclopedia, directories of hospitals and providers, surgical videos and links to the scientific literature. A "Go Local" feature links users to information about services in their communities. Today, there is go local coverage for approximately 44 percent of the U.S. population and expansion is an important goal for the Library in fiscal year 2010.

In 2009, the NLM celebrated its second year of producing the NIH MedlinePlus magazine, an outreach effort made possible with NIH and Friends of the NLM support. The free magazine is widely distributed to the public via physician offices, libraries, and other locations, with a readership of up to 5 million nationwide. A Spanish/English version, NIH MedlinePlus Salud (the Spanish word for "health"), was launched in January 2009 to address the specific health needs of the growing Hispanic population.

NLM also produces an array of specialized consumer health Web resources. Genetics Home Reference provides understandable information about genetic conditions and related genes or chromosomes. The Household Products Database provides easy-to-understand data on potential health effects of more than 2,000 ingredients contained in more than 8,000 common household products. The Dietary Supplements Labels Database has information from labels of more than 3,000 brands of dietary supplements, with links to authoritative sources of information.

ENSURING ACCESS TO INFORMATION IN TIMES OF DISASTER

NLM is committed to ensuring uninterrupted access to critical information services in the event of disaster or emergency. NLM's new Disaster Information Management Research Center is building on proven emergency backup and response mechanisms within the NN/LM to promote effective use of libraries and specially trained librarians—disaster information specialists—in disaster management efforts. The Center also collaborates with the Navy National Medical Center, Suburban Hospital Healthcare System, and NIH Clinical Center in the Bethesda Hospital Emergency Preparedness Partnership. The Partnership will provide hospital surge capacity for the national capitol area and create a surge model for use across the Nation. Recent studies found such capabilities lacking in major metropolitan areas. NLM coordinates R&D for this model and investigates new methods for sharing health information for disaster preparedness and response.

NLM also develops advanced information services and tools to assist emergency responders when disaster strikes. NLM's TOXNET, a cluster of databases covering toxicology, hazardous chemicals, and toxic releases, provides a foundation for services to first responders, such as Wireless Information System for Emergency Responders and Chemical Hazard Event Medical Management (CHEMM). CHEMM builds on the Library's successful collaboration with the HHS Office of Public Health Preparedness, the National Cancer Institute, and the centers for disease prevention and Control to develop the Radiation Event Medical Management (REMM) system. NLM is also developing a tool for identification of post traumatic stress disorder and mild traumatic brain injury.

In summary, the NLM is well-positioned to contribute to the Nation's health—by making increasing amounts of scientific data available to researchers and health practitioners, by improving the Nation's healthcare information infrastructure, by providing the public with access to authoritative information to maintain their personal health, and by enabling health sciences libraries to make substantial contributions to disaster information management. All of these activities will depend on a strong and diverse workforce for biomedical informatics research, systems development, and innovative service delivery. To that end, the NLM will continue its longstanding support for postgraduate education and training of informatics researchers and health science librarians.

PREPARED STATEMENT OF DR. JACK E. WHITESCARVER, DIRECTOR, OFFICE OF AIDS RESEARCH

Mr. Chairman and members of the subcommittee: I am pleased to present the President's fiscal year 2010 budget request for the trans-National Institutes of Health (NIH) AIDS research program of the NIH. The fiscal year 2010 budget includes $3,055,494,000, which is $45,155,000 more than the fiscal year 2009 appropriation of $3,010,339,000.

THE AIDS PANDEMIC

More than 33 million people around the world are estimated to be currently living with HIV/AIDS infection. More than 25 million men, women, and children have already died.

The pandemic affects the future of families, communities, military preparedness, national security, political stability, national economic growth, agriculture, business, healthcare, child development, and education in countries around the globe. As a result of multilateral and bilateral programs in low- and middle-income countries, almost 3 million people now have access to antiretroviral drug treatment. However, for every 1 person who starts taking antiretroviral drugs, another 3 become infected.

In the United States, HIV/AIDS remains an unrelenting public health crisis. The Centers for Disease Control and Prevention (CDC) reports more than 1.1 million people are infected with the virus, with approximately 56,300 new infections each year. According to CDC statistics, African-American men and women and gay and bisexual men of all races and ethnicities are the most affected groups in the United States. It is estimated that 1 out of every 20 individuals in the District of Columbia is HIV infected—a vivid example of the impact of AIDS on minority populations in the United States.

THE TRANS-NIH AIDS RESEARCH PROGRAM

The NIH AIDS research program is the largest in the world—a unique and complex multi-Institute, multi-disciplinary, global research program. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation. AIDS research is carried out by nearly all of the NIH Institutes and Centers in accordance with their mission. This diverse research portfolio requires an unprecedented level of scientific coordination and management of research. The Office of AIDS Research (OAR) was authorized to plan, coordinate, evaluate, and budget all NIH AIDS research, functioning as an "institute without walls," allowing NIH to pursue a unified research program to prevent and treat HIV infection and its associated complications. OAR has established comprehensive trans-NIH planning, portfolio analysis, and budgeting processes to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively and efficiently. The research priorities that frame this trans-NIH budget request were established through the annual OAR strategic planning process, involving scientists from NIH, other

Government agencies, academia, industry, and nongovernmental organizations, as well as community representatives.

FISCAL YEAR 2010 RESEARCH PRIORITIES: PREVENTION RESEARCH

Prevention of HIV infection is NIH's highest priority for HIV-related research. Disappointing results from recent clinical studies of HIV vaccine and microbicide candidates underscore the need for additional discovery (basic) research on HIV and the host immune response. Biomedical and behavioral interventions are urgently needed to reach individuals at risk, particularly in racial and ethnic populations in the United States, in international settings, among women, and among men who have sex with men. Priority areas include:

—*Microbicides.*—Microbicides, antimicrobial products that can be applied topically for the prevention of HIV and other sexually transmitted infections, may offer one of the most promising primary preventive interventions. NIH supports a comprehensive microbicide research program that includes the screening, discovery, development, preclinical testing, and clinical evaluation of microbicide candidates, as well as fundamental research aimed at understanding how HIV transverses mucosal membranes and infects cells. NIH supports behavioral and social science research on the acceptability and use of microbicides among different populations. In fiscal year 2010, NIH will increase funding for the design, development, and evaluation of microbicide candidates.

—*Vaccines*.—The best long-term hope for controlling the AIDS pandemic is the development of safe, effective, and affordable AIDS vaccines. AIDS vaccine research remains a high priority to ensure that new and innovative concepts continue to advance through the pipeline. NIH supports a broad AIDS vaccine research portfolio encompassing basic, preclinical, and clinical research. The disappointing results from clinical studies of the Merck HIV vaccine candidate indicate a critical need to reinvest in basic research studies on the virus and host immune responses that can inform the development of new and innovative vaccine concepts; as well as the development of improved animal models to conduct pre-clinical evaluations of vaccine candidates. In fiscal year 2010, NIH will fund additional basic research on HIV and host responses, as well as the design and development of new vaccine concepts and the pre-clinical/clinical development of vaccine candidates in the pipeline.

—*Behavioral Research*.—NIH supports research to further our understanding of how to change the behaviors that lead to HIV acquisition, transmission, and disease progression—including preventing their initiation—and how to maintain protective behaviors once they are adopted. In addition, NIH supports research aimed at better understanding the social and cultural factors associated with HIV risk or protection, particularly in communities at high risk of HIV acquisition. This research will contribute to the implementation of a broader range of preventive and/or therapeutic strategies.

FISCAL YEAR 2010 PRIORITIES: THERAPEUTICS RESEARCH

Antiretroviral treatment has resulted in improved immune function in patients who are able to adhere to the treatment regimens and tolerate the toxicities associated with antiretroviral drugs; and it has delayed the progression of HIV disease, extending the time between initial infection and the development of AIDS. However, a growing proportion of patients receiving therapy are demonstrating treatment failure, experiencing serious drug toxicities and side effects, and developing drug resistance. A critical area of research is the use of antiretroviral therapy as prevention. This includes evaluating the use of therapeutic regimens after exposure to HIV (postexposure prophylaxis), as well as testing the concept of the use of antiretroviral therapy in high-risk individuals prior to HIV exposure (pre-exposure prophylaxis).

Epidemiologic studies have revealed a number of co-infections and co-morbidities associated with long-term HIV disease, including tuberculosis, hepatitis C, malignancies, metabolic disorders, cardiovascular disease, and neurologic disorders. A better understanding of the underlying etiology of these HIV-associated conditions will lead to better prevention and treatment strategies. NIH supports a comprehensive therapeutics research program to design, develop, and test drugs and drug regimens to prevent and treat HIV infection and its associated co-infections and co-morbidities.

Translational and clinical studies also are needed to transform fundamental research results into improved strategies for preventing and treating these HIV-associated complications, including research on drug resistance, drug toxicities, pharmacogenomics, adherence, and the interrelatedness of HIV and nutrition.

DISCOVERY RESEARCH: ENABLING INNOVATION

A renewed emphasis on discovery research is essential to enable innovation, address critical gaps, and capitalize on emerging scientific opportunities. Groundbreaking strides have been made towards understanding the fundamental steps in the lifecycle of HIV, the host-virus interactions, and the clinical manifestations associated with HIV infection and AIDS. However, additional research is needed to further the understanding of the virus and how it causes disease, including studies to delineate how gender, age, ethnicity, and race influence vulnerability to infection and HIV disease progression. NIH-supported genomics studies and breakthroughs in sequencing the human genome provide new opportunities to apply these valuable tools to the search for new HIV prevention and therapeutics strategies. OAR proposes to capitalize on those opportunities by providing funds for new, exciting areas of investigation, including studies utilizing genomics tools to investigate the immune response to HIV infection.

RESEARCH TRAINING AND COMMUNITY OUTREACH

NIH must continue to support training programs for United States and international researchers to build the critical capacity to conduct AIDS research both in racial and ethnic communities in the United States and in developing countries. NIH funded programs have increased the number of training positions for AIDS-related research, including programs specifically designed to recruit individuals from underrepresented populations into research careers and to build research infrastructure at minority-serving institutions in the United States. The changing pandemic and the increasing number of HIV infections among women and in racial and ethnic populations of the United States, particularly in African-American and Latino/Hispanic communities, also underscore the need to disseminate HIV research findings and other related information to communities at risk.

SUMMARY

NIH-sponsored HIV/AIDS research continues to provide the important scientific foundation necessary to design, develop, and evaluate new and better vaccine candidates, therapeutic agents and regimens, and prevention interventions. NIH will continue to focus on the need for comprehensive strategies to decrease HIV transmission and improve treatment options and treatment outcomes in affected vulnerable populations in the United States, and in international settings. These interventions will address the co-occurrence of other sexually transmitted diseases, hepatitis, drug abuse, and mental illness; and consider the role of culture, family, and other social factors in the transmission and prevention of these disorders.

The NIH investment in AIDS research is reaping even greater dividends in unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases. AIDS research has provided an entirely new paradigm for drug design, development, and clinical trials to treat viral infections. Drugs developed to prevent and treat AIDS-associated opportunistic infections also provide benefit to patients undergoing cancer chemotherapy or receiving anti-transplant rejection therapy. AIDS research also is providing a new understanding of the relationship between viruses and cancer. We are deeply grateful for the support the administration and this subcommittee have provided to our efforts.

Senator HARKIN. Dr. Kington, thank you very much for your opening statement, and I see we've been joined by Senator Shelby.

Did you have an opening statement?

STATEMENT OF SENATOR RICHARD C. SHELBY

Senator SHELBY. Mr. Chairman, I'm glad to join you. I look forward to the hearing. I'll be in and out of here. We have some other Appropriations subcommittee hearings, but I do have a statement that I'd like to be made part of the record and I do have some questions that I'm going to have to leave and come back to ask those questions, unless you let me go.

[The statement follows:]

PREPARED STATEMENT OF SENATOR RICHARD C. SHELBY

Mr. Chairman, thank you. I appreciate you having this hearing today to discuss the vital mission carried out by the National Institutes of Health (NIH).

We live in a world where there are thousands of debilitating and life-threatening diseases—all that could use additional funding for research and clinical trials. We must continue to work towards the goal of increasing the overall Federal investment in basic research and development.

I support additional funding for NIH research, but in particular, I would like to emphasize today the importance of accelerating research in the area of Cystic Fibrosis (CF).

CF is a life-threatening genetic disease for which there is no cure.

But there is promise for people with CF—and that promise is in research.

Federal funding for medical research should accelerate the process of discovery and clinical development of new therapies for the treatment of disease. Yet, there is a significant discrepancy persisting between funding for clinical versus basic laboratory research.

Support for clinical research is particularly important for rare diseases, which often suffer from a lack of start-up funding needed to overcome the initial discovery phase of drug development and move into advanced stages of research.

Clinical research programs like the Cystic Fibrosis Foundation's Therapeutics Development Network have produced innovative new therapies for that disease. Led by research institutions including the University of Alabama at Birmingham, this national network allows multiple therapeutic approaches to be pursued simultaneously, accelerating the development of new treatments for the disease.

Dr. Kington coordinated networks such as the Cystic Fibrosis Therapeutics Development Network provide special insights regarding the most efficient means of conducting clinical trials.

Senator HARKIN. I have some, but, I mean, if you have to go to another——

Senator SHELBY. Senator Mikulski and I have a NASA hearing.

Senator HARKIN. Well, why don't you go ahead then? I'll hold mine and you go ahead and ask your questions.

CYSTIC FIBROSIS

Senator SHELBY. Thank you, Mr. Chairman.

Mr. Chairman, I thank you for the work you've done in chairing this subcommittee, and I continue to work with you.

We live in a world where there are thousands, everybody knows this, especially our panelists, we live in a world where there are thousands of debilitating and life-threatening diseases and they all could use additional funding for research and clinical trials, and I believe we must work toward the goal of increasing the overall Federal investment in basic research and development, and I applaud Senator Harkin in his work in this regard.

I personally, as a member of this subcommittee, support additional funding for NIH research, but in particular, today just for a few minutes, I would like to emphasize the importance of accelerating research in the area of cystic fibrosis.

Cystic fibrosis, as the panel knows, is a life-threatening genetic disease for which there is no cure but there is promise for people and that promise is in research.

Federal funding for medical research should accelerate the process of discovery and clinical development of new therapies for the treatment of this disease and others, yet there is a significant discrepancy existing between the funding for clinical research versus basic laboratory research.

Support for clinical research, as I understand it, is particularly important for rare diseases which often suffer from a lack of start-

up funding needed to overcome the initial discovery phase of drug development and move into advanced stages of research.

Clinical research programs, like the Cystic Fibrosis Foundation's Therapeutics Development Network, have produced in the way of new therapies for that disease. Led by research institutions, including the University of Alabama at Birmingham, this national network allows multiple therapeutic approaches to be pursued simultaneously, accelerating the development of new treatments for the disease.

Dr. Kington, coordinating networks, such as the Cystic Fibrosis Therapeutics Development Network, provide special insights regarding the most efficient means of conducting clinical trials.

Under your leadership, will the NIH increase Federal funding for these types of research?

Dr. KINGTON. Let me start off with a general answer and then I'll ask Dr. Nabel to comment, as well.

Senator SHELBY. Okay.

Dr. KINGTON. I think, in general, we agree that there are a lot of opportunities for us to accelerate the translation of scientific advances in the basic level into real treatments and interventions and diagnostic strategies at the bedside. We know that there are particular challenges for less common diseases.

In fact, we just announced yesterday a new initiative to help facilitate that translation and the Cystic Fibrosis community in many ways is held up as a good example of how a community affected by a disease can work collaboratively with the research community to facilitate translation and we're committed to helping that in any way we can.

Dr. Nabel, would you like to comment, as well?

Dr. NABEL. I appreciate your question. The NIH is very concerned about rare genetic disorders, like cystic fibrosis, and, indeed, I think if we can take a minute and really reflect upon the progress that's been made in cystic fibrosis, it's really been remarkable over the past decade.

We've gone from discovering the gene which causes the majority of cystic fibrosis, particularly the mutation, the CFTR gene. We know now that that gene leads to a protein that doesn't unfold properly. This protein is responsible for clearing secretion in the airways and in other tissues and when that protein doesn't unfold it can't lead to the clearance of secretions, mucous builds up, that gets infected and the sequela start.

What's very interesting is that the gene led to the understanding of what we call the molecular pathway that causes the disease. Understanding that molecular pathway then led to a search for new therapeutics that perhaps you're familiar with, and that search has now come up with two compounds, we call them small molecules, that are in clinical testing which directly affect the molecular pathway and, indeed, you probably saw Dr. Rootman's article in the New Yorker a couple of weeks ago and the remarkable report by several individuals who were enrolled in those trials saying how well they feel while taking these new drugs.

So that is, I think, a terrific example of how gene discovery leads to understanding, the molecular pathway leads to the detection of new therapeutics that are now being tested.

Can we do more in this area? Absolutely, absolutely. We're hoping to increasingly fund translational research and new clinical research in this area. The NHLBI currently has a specialized center for clinically oriented research in cystic fibrosis that's analogous to the CF Clinical Networks that you described and so many of those investigators are really the same community of folks.

But we look forward to really building and augmenting this research effort going forward.

Senator SHELBY. Well, I appreciate this. I know you have to start in the lab, but then you've got to move from the lab to the clinics to prove what's going on. So we have to have both, do we not?

Dr. NABEL. Absolutely.

Senator SHELBY. Well, I look forward to working with you, not just on cystic fibrosis, this is my attention for the moment, but in a lot of other diseases, and with Chairman Harkin in this regard.

Mr. Chairman, thank you for taking me out of order, but you know from chairing the subcommittee and being on other subcommittees, we sometimes meet at the same time.

Thank you, Mr. Chairman.

SUCCESS RATE OF ARRA

Senator HARKIN. Thank you, Senator Shelby, and thanks for all your involvement in this subcommittee over many, many years in research, medical research. So thank you very much for that.

Well, Dr. Kington, I want to talk about the Recovery Act and that money, and our budget. The problem is that the flip side of having all these requests come in is that most of them will not be funded. I'm hearing that the success rate for the Challenge Grants could be less than 5 percent.

So how do you keep up a high level of interest when so few researchers will actually get these grants? On the one hand it's a good thing. On the other hand do you discourage a lot of people when they don't get funded?

Dr. KINGTON. This is definitely a concern of ours. It's been interesting to read some of the press coverage which reporters have gone out speaking to scientists and we were pretty clear early on that we had a floor for dollars and that suggested that we would not have our usual success rate because this was a special program.

In spite of that, the scientists saw this as an extraordinary opportunity to actually get on paper interesting ideas in important areas. We believe that even with the substantial increase, I predict that we'll more than double that floor of $200 million, we still won't have a high success rate and there will be many good grants that we won't be able to fund, and there will be consequences for the agency and for the scientific community.

We anticipate that many of the scientists will resubmit those applications within our usual funding sequence. We suspect that we'll be able to fund some of them but our ability to fund even the very best of those applications will depend upon what our budget is in future years.

So it's a concern. I think at the very least it shows this extraordinary untapped supply of great ideas out there in the scientific community and I see that as a good thing.

ARRA AND FUTURE SUPPORT

Senator HARKIN. It seems to me that concerning the program you talked about, the Grant Opportunity Program, the GO Grants, it is my information that the purpose of this program is to support high-impact ideas that require significant resources for a discrete period of time to lay the foundation for new fields of investigation, Yet out of that $10.4 billion, $200 million is designated to GO Grants.

It seems to me that if you put most of the money in the RO1 grants and you do it for 2 years rather than 4 years, what happens after 2 years? Are you just sort of betting out on the cow that we're going to be able to keep that funding up? Because I'm not certain that we can.

I guess my question is, since this was a certain amount of money for a discrete period of time and you have these grants as I just defined them, why wouldn't I see more of that money going to that rather than RO1 grants for 2 years?

Dr. KINGTON. First of all, I think you'll see across the Institutes and Centers wide variation in whether or not—in how the dollars are distributed across these mechanisms and the numbers that we put forth were a floor.

I anticipate that the number will be higher because many Institutes, NHLBI and others, are increasing their commitments already to that stream of dollars and it will depend upon what ideas we see.

This was again a grand experiment in many ways to put out a broad call to see what the best ideas were and not restrict it to dollars, $1 million which was the limit for the Challenge Grants.

So the bottom line is that we think that we'll ultimately end up funding more than what we had initially planned. We believe that it's important to allow flexibility across Institutes and Centers. For some Institutes and Centers, these types of programs will be great opportunities. For others, scientifically it's a stronger case to fund more of the RO1s, but again even the RO1s, our estimate is that about, I think, one-third or so of the dollars probably will go to the existing pool of RO1s, but it varies from Institute to Institute.

Our goal is to make the framework as flexible as possible, but if we have great ideas, we'll put more resources toward the GO Grants and we are anxiously awaiting the applications. We anticipate that we'll get probably—I anticipate probably around 2,000 or so applications when all is said and done and if they're great ideas, we'll do our best to fund them.

Senator HARKIN. That's the GO Grants? That's what you're talking about?

Dr. KINGTON. Yes, the GO Grants, and again we suspect that many of these ideas that aren't funded but are still good will be resubmitted and our ability to fund those will depend upon what our budgets are in the out years.

We'll make the best decisions we possibly can to have the maximum impact of these dollars for science and public health, but again I see this in a very positive light, that we have had this extraordinary energized response by the scientific community.

It really is amazing, speaking to deans and faculty across the country, how excited the scientific community is both about the opportunities, the real opportunities to do work they otherwise couldn't have done, but perhaps even more importantly, about what these dollars said as a reflection of a commitment of the country to invest in biomedical research.

Senator HARKIN. Let me ask you this question. If, in the wisdom of Congress, it was decided that this money was to go out over 2 years, right?

Dr. KINGTON. Yes.

Senator HARKIN. But that's not to say we can't change our minds and it happens.

Dr. KINGTON. Congress can do whatever Congress wants.

Senator HARKIN. We can change our minds. It's occurred to me that, yes, we initially put that out there to be 2 years, but maybe we might want to think about making an exception for NIH, that maybe this money should be more than just a 2-year period of time.

Is that something that you could live with? I mean, would that help in any way or is it so set now for 2 years that we ought to just leave it alone? Rather than thinking about maybe changing it to provide for a longer period of time, say 4 years, to get that money out or something?

Dr. KINGTON. Well, we certainly made all of our decisions based thus far on a 2-year time horizon, but I will concede that having more flexibility probably would be helpful, but we also recognize the unique intent of these dollars and that is to stimulate the economy in the short run, and we believe we can responsibly spend the money in 2 years.

But some flexibility might help us as we sort of work through the process of spending. We might be able to have a benefit from more flexibility, but we will make good decisions even without that flexibility.

Senator HARKIN. Well, I might come back to you on that, not in this hearing but later on, to see if that flexibility might be the best course of action for us to take. Like I said, I don't know. It's just something I've thought about because again I just want to see how we judge the success of the Recovery Act funding.

I mean $10.4 billion within 2 years, but a lot of the results of that won't be known for some time. So I assume that a lot of people say we can judge the success on how many jobs it's created perhaps, if we're looking at it stimulating the economy. That's why the amount of money you put out there for extramural construction is important and getting new equipment in our labs is important, but I think a lot of the success of this will be judged, not just on the immediate jobs created but what's the long-term effect of the money that we provided?

So people say, "Did we get our money's worth?" Well, that's what's led me to think maybe—and I'm not saying this could happen—but maybe we ought to think about more flexibility in that 2-year time frame because I'm really worried. I say this to all of you. I'm really concerned about the cliff.

What's going to happen in 2011? We've got 2010, what 1.4 percent? 1.4 percent increase. You had it up there on the screen. But we funded $30.8 billion, but what happens in 2011 when—if all

these Recovery Act funds come out? I mean that's going to be a pretty hard landing, it seems to me, and, you know, I'm thinking about how do we soften that because I think we might be in a tough budget situation next year as we are this year and so since we've already appropriated this money for the Recovery Act, that we might think about trying to soften the landing a little bit. If you have any thoughts beyond that, of how we soften this a little bit, I'd like to know it, either today or maybe in writing or something later on.

Dr. KINGTON. We'd be happy to do that, and actually I'd welcome any of my colleagues. Just as all politics is local, all science is sort of local, as well, and many of—all of the Institute and Center directors are struggling with this exact same issue of how to responsibly make decisions now, recognizing the uncertainty about the future streams of dollars.

SUPPORT OF PROMISING RESEARCH AND FLEXIBILITY

Senator HARKIN. This is my chance to ask all of you here some questions. I'll start with Dr. Fauci.

Can you point to anything that your Institute is able to do now or can start and finish in 2 years? Is there something that you're able to do now with this Recovery money that you weren't able to do?

I'll ask each of you that. Dr. Fauci, any specific examples of research that you're able to fund that you otherwise might not have been able to?

Dr. FAUCI. Thank you for the question, Mr. Chairman. There are examples of things that we would not be able to fund if we didn't have it and there are examples of things that we can greatly accelerate and we would be able to use monies later on that we could continue it.

The example that I give is one of about three or four, and I'll only give one, is the money that we're putting in to accelerate the process of much more aggressive control of the HIV pandemic related to some novel and important research questions that need to be answered, as bold as trying to develop a functional cure for HIV to accelerating the process of what we call pre-exposure prophylaxis where you actually treat individuals who are in high-risk groups before they get infected.

There is a lot of research—it seems like a very interesting and important concept, but there are some very important research questions to be asked—Does it work? What is the relationship to adherence? Would it lead to resistance? If we can prove the concept, then that concept could transform how we prevent HIV infection.

And the last part of that triad is something that we call test and treat which the money for 2 years will help us accelerate the research endeavor in that we would not be able to do as quickly and we're committed to seeing it to fruition and the test and treat is a very bold concept that was put forth by a group at the World Health Organization about a half a year ago and that is to essentially test everybody and those who are infected, to actually treat them, regardless of where they are in the stage of the disease, with

the thought that if you get the viral load low enough, they will then not infect other people.

That is a very bold concept that will require globally a lot of resources, but the world is looking to the NIH to prove the feasibility of that concept and we're going to do that in a much more rapid way by the money that we have decided to use from the ARRA allotment to get that jumpstarted.

Senator HARKIN. You can't complete that in 2 years, surely, though, can you?

Dr. FAUCI. I might echo what Dr. Kington said. Flexibility in my mind is always something that would be helpful to us, but we still can get a lot done in the 2 years, but if we had more flexibility that would be advantageous to the program.

Senator HARKIN. Okay. Dr. Nabel.

Dr. NABEL. Thank you, Senator Harkin. I'm going to provide you one example of something that we couldn't do without the ARRA money and then another example of things that we can accelerate.

We will use ARRA monies as one-time money to expand our understanding of the genetics of complex diseases. I think this will apply across many of the Institutes but it will certainly apply to Heart, Lung, and Blood.

For example, over the years you've probably heard from NHLBI and ARRA, my predecessors, about the many large, what we call, cohort studies that the NHLBI has studied, the Framingham Heart Study, the Jackson Heart Study, our Hispanic Heart Study.

We've gathered beautiful clinical data for decades, in the case of the Framingham Heart Study 60 years. We now can take that data and combine it with the genetic understanding of the disease to gain new insights into the causation of blood pressure, cholesterol, asthma, COPD, and that's what we intend to do through some of our GO Grants, is to conduct more extensive genetic analysis of these large cohorts which you have helped us to support over the years. That's a one-time activity that we probably could not have afforded to do without the ARRA monies.

In terms of accelerating medical advances, I think Senator Shelby really hit the nail on the head. What we can do with the ARRA money is now begin to accelerate our translational research program. This infusion of money really helps us to focus on a number of mechanisms by which we can help our investigators speed, accelerate the basic advances into clinical trials and in fact, in terms of the Challenge Grants, I think our particular Institute, the last I heard, there was somewhere between 1,900 and 2,000 Challenge Grants just for the NHLBI.

We will supplement what Dr. Kington will fund from the Office of the Director, but many of these are focused on translational research and so we see this as an opportunity now to jumpstart.

We have one particular clinical trial, we call it SPRINT. For many years we thought the target for blood pressure lowering should be 140 over 80 but, you know, that might not be the right target. Maybe we should go a little lower. Maybe if we went lower, we could actually reduce some of the age-related effects of high blood pressure.

So SPRINT is to look at lowering down to 120 over 70, even 120 over 60 as the potential target. We want to look at this in adults

and, importantly, we want to look at this in our adolescents and our children.

You know one of the complications of obesity, many of our kids are becoming diabetic and hypertensive at a very young age and so this ARRA money will help us speed and accelerate the start of that clinical trial, extend it to a broader population, but yes, and then we'll need to fund the out years through appropriated dollars, but that's another example of a very important public health program that we can jumpstart, accelerate with ARRA monies.

Thank you.

Senator HARKIN. Dr. Niederhuber——

Dr. NIEDERHUBER. Thank you, Senator Harkin.

Senator HARKIN [continuing]. Tell us about cancer.

CANCER AND ARRA FUNDS

Dr. NIEDERHUBER. I think I'll echo flexibility. I think that would be helpful to all of us.

But we have some great opportunities, as you know, in terms of novel agents that have been developed but have not yet been able to move into the clinical trials arena, our early phase translational research, and so we're going to use a significant amount of these stimulus dollars, Recovery dollars to actually really jump into the clinic with early phase, first-in-man studies in a number of these new agents. I think that's going to have a significant impact.

Perhaps even more importantly than that is we have had a very successful pilot project that you're aware of, we call it TCGA, in which we've been actually developing the infrastructure to do complete sequencing of cancer. We've had three cancers in that pilot program, glioblastoma, ovarian cancer, and small cell lung cancer.

We've already found some extremely exciting discoveries in doing the sequencing, for example, of glioblastoma, genes that are related to that tumor that we didn't know were related to that tumor in the past.

I have a group of scientists meeting as we speak, yesterday and today, in San Francisco, that are analyzing our data on ovarian cancer and they tell me by phone some very, very exciting discoveries are coming out of that sequencing project.

So, clearly, this is telling us that the direction that we need to go in is to scale this up and that's what we're planning to do and the Recovery dollars will be a great help in our jumpstarting to do other tumors, to do them on a larger scale.

Without question, if we're going to repair this problem, we need to catalog all the defects and the technology is moving so quickly now that we will be able to do that and do that quite effectively over the next few years.

So these Recovery dollars are extremely important to our ability to really scale that up. It's true in cancer but it's true really in all of the diseases that you see here at the table and represented behind me.

RESEARCH PRIORITIES

Senator HARKIN. Okay. A couple of other areas I just wanted to cover with you today. Of the $442 million increase proposed for NIH, $268 million would go for cancer research, $19 million would

go for autism research. That leaves $155 million for everything else, heart disease, Alzheimer's, diabetes, AIDS, stroke, Parkinson's, on and on and on. I want to know if that makes sense.

You know, I know the statistics on cancer. I've fought as hard as anyone for more money for cancer research, but there are other devastating diseases, too, and we hear from these groups almost on a daily basis.

So when we're looking at a small increase, just 1.5 percent, should we put so much of that into just one disease rather than spreading it out more? So there you go.

Dr. Niederhuber, I don't mean to pick on you, but you're on the point on this. I'm saying, you've got a lot of the Recovery monies, but apart from that $442 million, I just question whether so much of it ought to go to two entities.

Dr. KINGTON. Why don't I start off?

Senator HARKIN. I'll leave that to Dr. Kington. Go ahead. Did you want to start off?

Dr. KINGTON. I'll take this one. As you noted, both cancer and autism are important public health challenges. These were priorities of the administration and the President and they're important priorities, and it's also important to note, though, that science in cancer is funded by every single Institute and Center. So it's not just Dr. Niederhuber. Every Institute and Center of the agency funds research related to cancer and we've initiated a strategic planning process, co-chaired by Dr. Niederhuber and Dr. Katz, to bring together all of the agency to think about how to develop a plan for increasing this investment in cancer.

It's also important to know that advances in cancer can help us learn more about basic biology in ways that would be useful for other diseases, as well.

Senator HARKIN. Well, that can be true of just about any disease.

Dr. KINGTON. That's absolutely true. Your point is well taken.

Senator HARKIN. So again, I'm back to square one. Is this a fair allotment of money? Any other observations on that? Do we have to decide ourselves how to allocate this money up here?

I just throw it out there because obviously we're trying to respond in a way to the legitimate interests of a lot of people out there suffering from these illnesses and we've made great advances in a lot of areas.

For instance diabetes, we have made some tremendous advances in diabetes research and others that I mentioned and taxpayers obviously have a right to question that we're putting all of the money in one area.

So I understand that, and I think that those of us here know that the administration proposed this, but we may have a different view on that. That's what I have to say about that.

OVERSIGHT OF OBJECTIVITY

Now, there are a couple of other things I wanted to bring up.

Last year my colleague, Senator Grassley from Iowa on the Finance Committee, requested some investigations into conflicts of interest. In fact, I just saw him this morning. We talked about it again, and he's still looking into that, his staff is looking into that, and we hear about it periodically. It comes up in the press or some-

thing like that, that some extramural researcher has gotten large payments from a private company that could be a potential conflict of interest.

In the fiscal year 2009 omnibus appropriations bill, I included a provision that required HHS to issue "an Advanced Notice of Proposed Rulemaking" which will start the formal process of revising the guidelines. The public comment period for that process started earlier this month.

So I was disturbed to see an article last week in The Chronicle of Higher Education in which an NIH official, I think unnamed, is quoted as saying, "We can't say definitely we would change the regulations."

Well, I don't know. Is that an authoritative statement? I hope not. I don't think that the present situation is working very well right now. So something has got to be changed here on this, Dr. Kington.

Dr. KINGTON. First of all, we absolutely share your commitment to having the agency playing a central role in assuring that there's objectivity in the science that we support which is the key issue here, assuring that first-rate science of the highest quality, objective science, is funded and produced.

We also recognize that there have been a number of cases of investigators that we believe may not have complied with our regulations and as almost all of the associations that have looked into this, as well, have concluded, we think that there are opportunities to strengthen our system of oversight.

The first step in that process is this Advanced Notice of Proposed Rulemaking and I think that the quote—well, I know the quote was taken out of context because, technically, the whole point of starting this process is to ask the question and for us to presume at the beginning the answer might raise serious questions about the whole process and so I think it was a technical response.

I think we've said, I've said personally in a number of settings, as well, that we believe that there are opportunities to strengthen our system of oversight. There are things that we're doing within our current regulation to do just that—increase training and education and strengthening our reporting system. There are lots of things that we're doing now to change fundamentally and improve the way we oversee management of conflicts of interest.

We're committed to doing that in the future and we will take seriously all the comments that we anticipate receiving under this Advanced Notice of Proposed Rulemaking and we're committed to doing the right thing.

Senator HARKIN. Well, I appreciate that. I think we have to be more positive in our approach on this, and on looking at these potential conflicts of interest.

I've been on this subcommittee a long time and I know how difficult it is sometimes because a lot of research is paid for by the private sector, by the private drug companies, and it's good, valid research, and so how do you divide a researcher that has an institute—not an nstitute, but has a lab and they're getting some private money in and—but then they also qualify for an NIH grant. How you separate that out sometimes is pretty darn difficult. So I understand that.

I'm more interested in the conflict of interest in which a person receives monetary income for their own bank account. I'm not so much interested in the lab itself and that money. I'm interested in what an individual might get paid by a drug company or something like that and when they are looking at certain drugs, for which they then recommend certain courses of action.

This has to do with, I think, anti-psychotic drugs mostly and that this individual had been involved in researching it but also—maybe this is a bad choice of words, but promoting the use of these anti-psychotic drugs.

I bring this up because I know that my colleague, Senator Grassley, is going to continue to look at this, as he should, and we have to. We have to be cognizant of this issue and do our best to answer those problems.

Dr. KINGTON. Yes.

H1N1 FLU

Senator HARKIN. The other thing I wanted to ask, Dr. Fauci, and it's sort of a replay of what we went over a couple weeks ago when you were up here, this H1N1.

Where are we now? What are you seeing? Is it kind of dwindling now here?

There was some talk that it might move to the Southern Hemisphere because of wintertime there, then it might come back here again this winter in a more virulent form. I keep wrestling with this problem of developing a vaccine because some of the money that we put in this was to develop a new vaccine. But again if we develop a new vaccine for the H1N1 strain that we see now, but then it comes back this fall and it's different, how are we going to be certain that the vaccine we develop this summer is going to be effective against the strain of flu that might come back this fall?

I'm still wrestling with that. I still don't understand that.

Dr. FAUCI. Okay. So three questions you asked me.

Senator HARKIN. Okay.

Dr. FAUCI. The status, vaccine, and does it change?

Senator HARKIN. There you go.

Dr. FAUCI. Okay. The status of the outbreak right now is that there's still considerable flu activity with H1N1 in the United States and worldwide. A recent outbreak that you read of, I know, in Japan. So there's considerable activity still going on.

The CDC estimates that even though there are about 6,000 reported cases that are confirmed or probable in the United States, it's likely that there are close to 100,000 people that have been infected. You don't pick them up because much of the illness is mild illness, yet there are some serious cases, which causes us to have an appropriate amount of attention to following this.

As I mentioned to you a couple of weeks ago, this is a brand-new virus. It's an H1N1 but a different kind of an H1N1. It has swine origin as well as some avian and human origin. It is brand new. So the inherent unpredictability of influenza is compounded by the fact that we're dealing with a virus that we've never had any experience with before.

Fortunately for us, we're going into a summer season when the conditions, the physical conditions for the spread of an influenza

are minimized, but that doesn't mean that we still are not going to have some considerable problems.

So the bottom line is that this outbreak is still in a dynamic stage and it's not over for us yet for the immediate period of time.

What about the concern of what it might do? The fact that it's out there and it has already manifested its ability to spread from human to human here in the United States, Mexico, Canada, Europe, Japan, et cetera, that the concern is that we have to watch this very carefully from two standpoints.

What happens in the Southern Hemisphere in the next month or two when they enter into their fall and winter, and we're going to watch that very closely because it will tell us what might happen to us next fall and winter for our seasonal flu vaccine time. The reason is that what usually happens, not always but usually is that the Southern Hemisphere flu activity is generally a good reflection of what might happen to us in the Northern Hemisphere in the following season. So we're looking at that very, very carefully.

VACCINES

Vaccine. The process of developing a vaccine has already begun and as I mentioned to you before but just to reiterate it very briefly, it's a multistep process and there are points in that process where there's a decision point, a go or no go.

The first thing you do is you isolate the virus. That's been done. You start to grow it up as a reference strain or seed virus. The CDC is very actively involved in this and should have seeds ready to go out within a reasonable period of time. The prediction is by the end of this month. Hopefully that will be on time.

Once that goes to the pharmaceutical companies, then they make pilot lots for clinical trials which is where the NIH comes in because then we have to ask the question: is it safe, does it induce an immune response that would be predictive of being protective, and what's the right dosage and the number of doses? At the same time, the companies will then start to, were the decision to be a go decision, to start to scale up.

Your concern that bothers you is that if we're starting to make a vaccine for a virus that's circulating now and would likely return again in the fall and winter, what happens if it changes?

Senator HARKIN. Yes.

Dr. FAUCI. That's always a possibility. The likelihood of it changing so much that a vaccine that we're making now would be essentially noneffective is small, not zero, but it's small. That's the reason why the way we set it up in the department with the CDC, FDA, and the NIH is for multiple decision points along the way whether to make it, how much to make and whether to administer it.

I will point out to you that every year when we make a vaccine for seasonal flu, put aside the pandemic for a moment, there's always the risk that the vaccine that you decide to make, that what happens to you the next season, it will change enough not to make a vaccine as effective as you want.

Historically, most of the time we get it right. So we are hoping that we will get it right. I think we will. I don't think there will be that much of a change, but as I mentioned, influenzas are char-

acterized by their unpredictability, but you've got to go with the science that you have, and the science that we have now tells us that this virus that's out there hasn't really changed much over the months that we've been following it.

It started off in Mexico, the first detection in Mexico. We don't know where it started, but the first detection was somewhere in March or so. So we're now a few months into it and the virus seems to be pretty much the same as it's been. It's stayed relatively stable. That doesn't mean it's going to stay that way over the next year, but it has not drifted a lot.

Senator HARKIN. I keep hearing that even the seasonal flu vaccine may offer some immunity.

Dr. FAUCI. No.

Senator HARKIN. No?

Dr. FAUCI. No. This is good news for you, Senator, and me, and that is, it doesn't have—the vaccines that have been used seasonally don't appear to induce antibodies that strongly cross-react at all with the H1N1 that's the new novel H1N1.

But what we are observing is that in the community this virus seems to be selectively more preferentially affecting young people. So the question is, Do old people—older people—have in their body some antibodies or cell-mediated immunity that they acquired from previous exposures to H1N1s over the previous years that are a bit below the radar screen, but that seem to be giving some protection? That's one of the prevailing theories, not proven yet, of why we're seeing it much more in young people.

In fact, when you measure the antibodies in older individuals, a rather significant percentage of them have some cross-reactivity with the virus that's circulating now and the most obvious, though not necessarily proven, but the most logical reason for that is that they've been exposed over the last few decades to an H1N1 that has some similarity to the H1N1 that we're seeing now.

BARKER HYPOTHESIS

Senator HARKIN. Well, I'll have to correct some of the ways I've been saying things then because I've been led to believe maybe some of the immunities we have comes because we've gotten the seasonal flu shots over the last few years, but that's not it. It has to do with our exposures to the influenza virus some time in the past and we've developed antibodies to it. I'll have to correct the way I say that now.

There's only one other area I just want to get into.

First, you all know that we've been working very hard on healthcare reform and the area that I've been involved in, of course, and I've been harping on this for many years is getting into prevention and wellness and focusing on that. I think we're going to have some, I hope, great success in the health reform bill in moving in that direction, which leads me to this next question, and it has to do with some of the information my staff has given me and I've been reading about it, the so-called Barker Hypothesis.

Dr. Barker of Oregon Health and Science University, who did a study that was very interesting—no, sorry, he didn't do a study. He examined other studies and came to some interesting conclusions,

that pre-natal care—how you're taken care of before you are born may have a great impact on what happens to you later in life.

My first initial reaction when I read that was, of course, if you have a low birth weight baby that means you don't get the right kind of nutrients and support during pregnancy. This happens sometimes in poorer families. I can understand that.

But then evidently Dr. Barker factored that in and had accounted for that in his studies. And even accounting for that, it shows up that if you have a low birth weight baby, there were certain twins they followed the one that had the low birth weight had the most problems later on in terms of diabetes, stroke, hypertension, all kinds of things.

So I guess my question is to maybe any body sitting there is, are we doing research? I've just come across this in the last few months and I wonder, are we looking into this? Is NIH doing any research in this area?

Dr. KINGTON. Yes, we are. David Barker is a British physician who in the 1980s began to notice patterns of tracking of looking geographically at mortality rates in England, patterns of mortality that tracked adult cardiovascular mortality with infant birth weight and that was the beginning of this long line of research that has been supported by the agency, including by NICHD, and there are a range of evidence, some—most supported but some not supported, of this hypothesis that has evolved into a more complicated discussion about potential ways in which the intrauterine environment sort of sets trajectories by turning on or off genes or somehow setting trajectories that actually are manifest in late life but start off this trajectory.

The hypothesis is that there's something unique going on in these early stages and it has implications for this entire continuum of potential causal pathways, from smoking now all the way back to shortly after conception and what happens in the intrauterine environment.

It's an interesting hypothesis and generated a great deal of discussion, both in Europe and in the United States, and we fund research related to it. I think it's still to be determined what the implications are for intervention and what we do clinically, the argument being that if we know more about what happens in the intrauterine environment, we might intervene in ways beyond the obvious of good nutrition and prevention and all the things that you noted, better social environments and all the things that we know are good for starting off children beginning healthy lives.

So the jury is still out about what the implications are, if it's correct, and there's a growing evidence base both in humans and in animal models, and we're supporting research and looking forward to seeing more advances in this area and we'd be happy to sort of synthesize some of the findings that we've supported and get back to you about that, as well.

[The information follows:]

THE BARKER HYPOTHESIS

David Barker, an English epidemiologist working at the University of Southampton, noted that the geographical regions of the British Isles reporting high rates of death from coronary heart disease were the same regions that reported high rates of low birth weights. In a landmark study published in the medical journal Lancet

in 1989, Dr. Barker and his colleagues reported on an analysis of serial data collected on 5,654 men in Hertfordshire. They found that the men with the lowest weights at birth had the highest death rates from coronary artery disease. Those with the lowest birth weights had more than twice the mortality rate than those with the highest birth weights.

In seeking to explain the remote outcomes of low birth weight, Dr. Barker developed the Barker Hypothesis, which states: environmental factors that impair growth and development during fetal life and early infancy are risk factors for hypertension, type 2 diabetes, stroke, and coronary disease later in life.

A general explanation for these findings is that birth weight represents an integral of all events that affect development during gestation, including nutrient supply, vascular sufficiency, infection and stress. The key question is to determine mechanistically what happens to the fetus to alter permanently its physiology and metabolism throughout later life.

Studies in animal models are useful in revealing the physiological connections between impaired intrauterine growth and chronic disease later in life. Dr. Lori Woods at the Oregon University of the Health Sciences has shown that reduced maternal protein intake in a rat model impairs the development of the kidney in the offspring, leading to hypertension later in life. In a baboon model Dr. Peter Nathanielsz at the University of Texas at San Antonio has shown that nutrient restriction during fetal life leads to impaired development of insulin manufacture by the beta cells of the pancreas, predisposing the animals to type 2 diabetes later in life.

The most widely accepted mechanism that explains these relationships is the metabolic adaptation that the fetus makes to survive in an intrauterine environment impaired by nutrient insufficiency, such as an increased secretion of cortisol. The survival mechanisms that are useful in the uterus, however, are maladaptive in a plentiful nutritional environment after birth as reported by Barker and his colleagues in two articles in the New England Journal of Medicine in 2004 and 2005. The first showed that low birth weight babies in an East Indian population who gain weight rapidly after birth are at high risk of developing type 2 diabetes in their third decade of life. The second showed that Finnish boys and girls with low birth weight are at increased risk of coronary artery disease later in life, especially those whose tempo of weight gain is greatest in the first decade of life.

The Barker Hypothesis has stimulated new fields of related research on the effects of inimical environmental influences on the development of the brain and body during fetal life and early childhood. One line of investigation suggests that overnutrition during pregnancy also can have untoward effects on offspring later in life. The NIH Obesity Research Task Force has identified this area as a research priority in regard to the development of type 2 diabetes, lipid disorders, and other metabolic disease in offspring. Studies in nonhuman primates have shown that consumption of a high fat-high calorie diet during pregnancy results in extensive fatty liver disease in the offspring, a disorder being seen with increasing frequency in obese adolescents. Maternal obesity has been reported to increase the risk of congenital defects, particularly neural tube defects, in developing offspring.

Other studies suggest that high levels of blood sugar during diabetic pregnancies affect an offspring's risk of obesity and type 2 diabetes later in life. NIH intramural investigators have shown in the Pima population of Arizona that type 2 diabetes in the mother leads to increased risk for type 2 diabetes and obesity in the offspring. Adverse effects of intrauterine exposure to diabetes were also shown recently in a racially and ethnically diverse population of youth; the NIH- and CDC-supported SEARCH study found that children with type 2 diabetes received their diagnosis at an earlier age if their mothers had been diagnosed with diabetes prior to pregnancy.

Another interesting line of research stimulated by the Barker Hypothesis involves the influence of maternal infections and intrauterine exposure to environmental agents on the development of disease in the offspring later in life. Dr. Alan Brown and colleagues at Columbia University have shown that maternal infections with strains of influenza virus type A and B during the first trimester of pregnancy increase the risk of schizophrenia spectrum disorders in the offspring later in life. They also showed a similar effect of maternal infection with toxoplasmosis. Preliminary, unpublished studies by Cohn and colleagues of the Public Health Institute in Berkeley, California, show an association between maternal serum levels of dichlorodiphenyl-trichloroethane and testicular cancer in male offspring later in life. The National Children's Study, currently under way, is designed to assess the effects of such environmental exposures during pregnancy and early childhood on many other aspects of health and disease later in life.

In sum, the Barker Hypothesis, now 20 years old, has led to numerous productive lines of research which have relevance to many NIH Institutes, including the

NICHD, NIDDK, NCI, NINDS, NHLBI, NIEHS, NINR, NIDA, NIAAA, NIAID and the NIMH.

WELLNESS AND PREVENTION

Senator HARKIN. I'm just curious. What Institutes would be the lead?

Dr. KINGTON. Child health, I know, has funded. Aging has funded some, as well, because some of the early studies—the intriguing idea was that something happening in the uterus would be manifest in old age and some of the interesting studies focused on that element of this relationship.

Senator HARKIN. Do you have any idea about when we might be able to really get some body of evidence or something that we could rely on to say for prevention, we ought to be doing this and that pre-natal care and pregnant women ought to take certain factors into account?

I don't know that we have enough to go on right now. I don't know. Do we?

Dr. KINGTON. That's the point. I don't think we've resolved the scientific question enough to translate into a different way of doing what we're doing now, which is a lot of the things that you noted, good nutrition, all the prevention things that we know, pre-natal care, the social environment of pregnant women, all the things that we know are very important for having healthy babies.

I don't think that the science is at a point where that would tell us to do something different or beyond what we know now as best practice. I think we're still ahead of the curve on that, but we're funding research and interesting ideas. It's been bandied about for a couple decades now and the evidence base was growing, not uniform support, but an evidence base and an interesting problem and question.

Maybe Dr. Nabel might want to comment, as well.

Dr. NABEL. Yes, I think the Barker Hypothesis raises in a broader term the concept of when should we begin prevention measures. I think that's probably one of the points you're getting to.

From the cardiovascular and from the diabetes and obesity literature, we do know that the intrauterine environment makes a distinct difference in terms of predisposition toward subsequent diabetes and obesity in the newborn, but it also raises the fact that there's growing recognition among physicians, healthcare providers, that rather than waiting until middle age to focus on risk factor detection and prevention, we've got to shift much earlier and initially we shifted to the young adulthood but now we're increasingly more and more shifting to adolescence and childhood.

In fact, the American Academy of Pediatrics has put out guideline recommendations for detection of cardiovascular risk factors, for example, in pediatric population.

So there's growing recognition. Much of that recognition is built on the science base, that we're beginning to see, serendipitously, risk factors appearing in the pediatric office. When we go back and do natural history studies or observational studies then we can detect it on a scientific level.

So yes, we know that these risk factors are appearing much earlier in life and that now is leading to action programs for detection and risk factor management.

Senator HARKIN. Very good. This is the last one, I promise, but I did want to get this in.

Dr. KINGTON. You may ask as many questions as you like.

COMPARATIVE EFFECTIVENESS RESEARCH

Senator HARKIN. It has to do with comparative effectiveness. Dr. Nabel, this is probably to you.

We provided $1.1 billion for comparative effectiveness in the Recovery Act. I have to admit, I did that and I have a lot of people asking about that. We put $400 million in there and that money is going to be used by NIH.

We also created the Federal Coordinating Council for Comparative Effectiveness Research (CER), which will recommend priorities for this research and I understand you're a member of this Council.

Again, can you tell me something about NIH's plans for the $400 million? What kinds of activities might fall into the category of comparative effectiveness research as far as NIH is concerned? What are you looking at and what are you going to use that money for?

Dr. NABEL. Terrific. Well, thank you, Senator, for the question.

As you know, the NIH has supported work that now fits the definition of comparative effectiveness research for many years, but we're delighted to have this additional money to again do things that we normally could not do or to jumpstart or accelerate other programs.

Dr. Richard Hodes, the Director of the Aging Institute, and I co-direct the NIH Comparative Effectiveness Research Coordinating Committee. This is a committee that has brought together senior leadership, Institute Director leadership and deputy director leadership from across the agency to develop plans for that $400 million and again we're enormously grateful.

We are looking at opportunities now that meet the definition of CER and would allow us to conduct research that again will either—something that we normally couldn't do or would jumpstart.

We are looking at several possible mechanisms for supporting that research. One are payline expansions, so studies that Institutes have had to leave on the table because they simply did not have enough funds to initiate it. We're looking at the possibility of supplements that could accelerate enrollment in a trial or add an ancillary study or accelerate a trial in another way.

We anticipate that over the summer we will have a broad number of Challenge Grants because in fact CER was one of the Challenge Grant topics. We anticipate we will have applications in CER, and we also anticipate there may be some GO applications that also meet the definition of CER.

So we continue to meet on a regular basis. We are coordinating our work with the work of AHRQ and the Federal Coordinating Committee. We are working toward one common definition of CER for the department which we anticipate using and we are very cognizant of the fact that we want to make good use of this money. We want to get it right.

We see this as a downpayment toward many CER activities that we would like to continue in the future.

Senator HARKIN. I wanted to get that on the record and thank you very much for your response on that.

I have no further questions. Do you have anything else that any of you would like to bring up before we close this down?

Well, let me just say thank you to all of you and to all of you in the row in the back and to all the Directors of the Institutes.

Again, NIH is just one of our shining examples, I think, of good public policy and what we're using taxpayer dollars for and for all the years I've been privileged to associate with you, I just think you're doing an outstanding job at NIH, all of you.

I thank you very much for your commitment to public service and to public health and to the research that we do at NIH and I always like to continue to say for the record that this is the National Institute of Health. It's not the National Institute of Basic Research. Basic research is important, but we always have to keep in mind we are looking at increasing the health of our people and of humankind in general. It's not just geared toward the American people, and so with all of that research we have to keep thinking about, what's that translational research, what's it going to translate into? Better health for people and I think NIH has done an outstanding job in that through all its years.

So again, my thanks for your public service. I would again say, Dr. Kington, that I just repeat what I said earlier, I'm hopeful that this fall I will have healthcare reform behind us, maybe a little bit more time. It would be my intention and my desire and my intention to reprise again what we did a couple years ago. I'd love to have the Institute Directors down, two or three at a time, for some in-depth look at what the research is doing.

ADDITIONAL COMMITTEE QUESTIONS

I think it's not only good for the record but I think it's good for us to know, me and the staff and the others who are charged with the responsibility of making some of these decisions to know exactly where we are and where some of the new research avenues that are going on in all these different Institutes. So I hope to be able to do that some time this fall.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR TOM HARKIN

PANCREATIC CANCERS

Question. Dr. Niederhuber, one of the deadliest forms of cancer—pancreatic cancer—also seems to be one of lowest priorities of the National Cancer Institute (NCI). Pancreatic cancer research accounts for less than 2 percent of the Institute's budget. Last year, the subcommittee asked for a report on how resources will be used to address this problem. Would you tell us what, if anything, is being done to expand the research portfolio for this lethal form of cancer?

Answer. NCI is committed to pursuing a broad research effort for pancreatic cancer. In 2001, NCI convened a Pancreatic Cancer Progress Review Group (PRG) to identify priority areas for research. Since that time, NCI's support for pancreatic cancer research has grown significantly. Based on the recommendations in the PRG report, NCI expanded its portfolio of pancreatic cancer research from $21.8 million in fiscal year 2001 to $87.3 million in fiscal year 2008. Part of this growth came

about through planned actions and funding opportunities specific to pancreatic cancer, and part grew out of an increasingly larger pool of pancreatic cancer researchers successfully competing for general funding opportunities and unsolicited research grants.

In the past 7 years, the number of investigators funded through the standard principal investigator-funding R01 awards has more than doubled, increasing from 34 to 93. The total number of research awards with a pancreatic cancer focus has more than tripled since fiscal year 2000, increasing from 85 projects in fiscal year 2000 to 271 projects in fiscal year 2007.

NCI has also increased the number of Specialized Program of Research Excellence (SPORE) grants with pancreatic cancer components, increasing the investment from one award in fiscal year 2000 to a total of six in fiscal year 2008. SPORE grants support specialized centers that promote interdisciplinary research, moving basic research findings from the laboratory to clinical settings while also bringing clinical findings back to the laboratory environment. SPORE investigators work collaboratively to plan, design, and implement research programs that may impact cancer prevention, detection, diagnosis, and treatment. Five of these SPORE grants were initially awarded shortly after the PRG meetings were held, with the sixth SPORE newly awarded in fiscal year 2008.

NCI continues to support pancreatic cancer research training awards for graduate students, postdoctoral trainees, clinical researchers, and junior faculty, as well as career transition and development awards for established investigators. In fiscal year 2005, an estimated 23 distinct training projects were relevant to pancreatic cancer research and approximately $2.2 million was spent on these projects. In fiscal year 2006, an estimated 31 distinct training projects were relevant to pancreatic cancer research and approximately $2.7 million was spent on these projects. In fiscal year 2007, an estimated 36 distinct training projects were relevant to pancreatic cancer research and approximately $2.8 million was spent on these projects.

NCI implemented a policy in fiscal year 2002 of increasing its payline (percentage of applications that are funded) for research that is related to pancreatic cancer. Initially, NCI's policy called for a 50 percent higher payline for investigator-initiated R01 grant applications with 100 percent relevance to pancreatic cancer. Since fiscal year 2004, grant applications with 50 percent or greater pancreatic cancer relevance were given special consideration for exception funding.

NCI has also developed pancreatic cancer-focused initiatives, including the Pilot Studies in Pancreatic Cancer and the Pancreatic Cancer Cohort Consortium. The Pilot Studies promote innovative multidisciplinary research to increase our understanding of pancreatic cancer biology, etiology, detection, prevention, and treatment. The Pancreatic Cancer Cohort Consortium is a group of investigators from 12 prospective epidemiologic cohorts and 1 case-control study who conducts whole genome scans of common genetic variants in order to identify markers of susceptibility to pancreatic cancer. Pancreatic cancer studies have also been funded within the Mouse Models of Human Cancers Consortium, Novel Technologies for In Vivo Imaging, Cancer Nanotechnology Platform Partnerships, and the Early Detection Research Network.

The Pancreatic Cancer Research Map is a Web-based tool developed for tracking pancreatic cancer research, clinical trials, and investigators. By providing a way to search the pancreatic research portfolio for funding opportunities, investigators, and developments in pancreatic research, the map facilitates and expedites collaborations and networking among researchers focuses on this disease.

Recently, as part of the restructuring of the NCI Clinical Trials Enterprise, NCI formed the Gastrointestinal Intergroup. Pancreatic cancer is one of the gastrointestinal cancers that the group will be looking at as they harmonize an efficient, cost-effective, science-driven, and transparent process that will identify and promote the "Best Science" in gastrointestinal cancer clinical research by addressing the design and prioritization of large phase II studies and phase III trials in these cancers.

PROGRESS IN TREATMENT AND PREVENTION OF PANCREATIC CANCER

The number of therapeutic trials that can be conducted in any cancer type depends upon scientific opportunity, frequency of the disease, and its outcome. NCI has been able to test a large number of drugs intended to treat pancreatic cancer in small trials. Unfortunately, as you know, to date pancreatic cancer has proven to be unresponsive to most drugs and radiation therapies. Less than 20 percent of patients with pancreatic cancer are candidates for surgery, because the disease is often detected in the late stages. Gemcitabine has been a standard treatment for patients with advanced and inoperable pancreatic cancer for a decade. New findings support use of the chemotherapy drug in the adjuvant setting, and patients who re-

ceived the drug gemcitabine after surgery for pancreatic cancer lived 2 months longer than patients who had surgery alone. This study shows that this treatment improves a patient's survival and more than doubles the overall survival 5 years after treatment.

Another study has shown that a new drug combination tested in mice may target the cells responsible for driving some pancreatic tumors. The combination of gemcitabine and the experimental drug tigatuzumab eliminated populations of cancer stem cells and reduced tumor growth in a mouse model of pancreatic cancer. The results provide a rationale for testing the promising combination in patients with this deadly disease. Tigatuzumab is also being tested in a phase II clinical trial with patients who have inoperable, untreated pancreatic cancer.

Ultimately, only a better understanding of the genetics and biology of pancreatic cancer is likely to yield improved therapies. These fundamental breakthroughs are likely to be produced by basic and genetic research into the mechanisms of cancer risk, initiation, growth, and resistance, in which NCI is heavily invested. One such investment is PanScan, a project made up of 12 cohort and 8 case-control studies primarily supported by NCI. The goal of PanScan is to identify the genetic variants that increase the risk of developing pancreatic cancer and refine our understanding of the interactions of tobacco and other nongenetic risk factors with the genetic variants that increase pancreatic cancer risk.

NCI anticipates that these studies will provide fundamental new insights into the genetic underpinnings of pancreatic cancer similar to the recent discoveries resulting from the genome-wide scans of prostate and breast cancers. These findings will inform further biological research that is likely to have clinical applications, including the detection of molecular targets for preventive, diagnostic, and therapeutic interventions. It is expected that the initial findings this study will be published later this year.

NCI is also involved in the Pancreatic Cancer Genetic Epidemiology (PACGENE) Consortium which was developed to identify susceptibility genes in familial pancreatic cancer. The Consortium consists of seven data collection centers, a statistical genetics core, and a pathology/archival genotyping core. PACGENE recruits people with two or more affected blood relatives found through incident pancreatic adenocarcinoma cases, physician referrals, as well as Internet recruitment. Accrual to a database containing core clinical, demographic, lifestyle and family history information from questionnaires is ongoing, along with biospecimen collection. The shared goals and methodologies of data collection of this Consortium will facilitate and accelerate our understanding of the genetic basis of pancreatic cancer.

In addition to genetic research, NCI is also supporting pancreatic cancer research that utilizes nanotechnology. Cancer Nanotechnology Platform Partnerships, a component of NCI's Alliance for Nanotechnology in Cancer, are developing technologies for new products in such areas as molecular imaging and early detection. One partnership is studying the use of nano particles in the diagnosis and therapy of pancreatic cancer, and developing and testing nano particles that will deliver imaging and therapeutic agents to pancreatic tumors.

PREVENTION

There are presently no effective ways to detect early signs of pancreatic cancer. One way to discover susceptibility genes for an inherited disease is to analyze DNA from large families with many affected members. But this strategy does not work with inherited forms of pancreatic cancer, because the disease is so deadly that there are very few large families with adequate numbers of samples.

Researchers at the Johns Hopkins Kimmel Cancer Center have shown for the first time that sequencing the genes in both the normal and the cancer cells of a single patient can reveal genes that are altered in both types of cells. Some of these changes can help identify susceptibility genes.

This strategy offers a new way to find hereditary susceptibility genes, and in the future, these genes could be part of a panel used to evaluate patients with familial pancreatic cancer. A test for predisposing mutations could help identify people at high risk of the disease who could be monitored for precancerous changes, enrolled in screening programs and potentially prevent them from getting pancreatic cancer.

Question. In addition to pancreatic cancer, would you tell us how NCI plans to attack some the other deadly cancers—ones where survival rates remain low?

Answer. In terms of other deadly cancers, the following are the ones with the lowest percentage for 5-year relative survival rate (30 percent or lower).

OVARIAN CANCER

The high-mortality rate stems from an overall lack of early symptoms or screening methods for the disease. As a result, most ovarian cancer patients are diagnosed with advanced stage disease. For fiscal year 2009, NCI is funding 5 SPORE program grants, and the relatively low incidence of this disease, as well as the team concept of the SPORE program, has resulted in a number of Inter-SPORE activities aimed at developing much needed early detection, screening, prevention, and therapeutic tools for ovarian cancer. These supplemental activities are being performed in collaboration with a number of other NCI programs, including Avon Progress for Patients Partnership, the Cancer Genetics Network, the Early Detection Research Network, the Division of Cancer Prevention's Prostate, Lung, Colon, and Ovarian Cancer (PLCO) Screening Trial and the NCI Intramural Program.

The Cancer Genome Atlas (TCGA) is assessing the feasibility of systematically identifying the major genomic changes involved in cancer using state-of-the-art genomic analysis technologies. Ovarian cancer is one of the first cancer types to be studied in the TCGA pilot phase. Early results are revealing genetic changes that could be used to identify those women who may be at risk for developing ovarian cancer, as well as pointing to markers for early detection of the disease when there is a better potential for successful therapy.

NCI's Cancer Nanotechnology Platform Partnerships are developing technologies for several key areas including studies focused on developing multifunctional nanoparticles that can deliver light-activated anticancer compounds specifically to ovarian cancer cells through a partnership at the Massachusetts General Hospital.

The New Drug Combination for Ovarian and Primary Peritoneal Cancers clinical trial is testing the combination of cisplatin, a drug containing platinum, and flavopiridol, which blocks the activity of proteins that help cancer cells grow and spread, in women with ovarian or peritoneal cancer resistant to platinum-based chemotherapy. Flavopiridol can increase the platinum concentrations in cells when administered with cisplatin, and researchers believe that this may lead to a reversal of platinum resistance.

The National Ovarian Cancer Early Detection Program.—Screening and Genetic Study is determining effective screening and genetic testing methods to identify women at increased risk of ovarian cancer. The study is also designed to develop markers for early detection and novel therapies.

LIVER AND BILE DUCT CANCER

Primary liver and bile duct cancers are the fifth most common cause of cancer death in men and the ninth most common cause of cancer death in women. More than 90 percent of all cases occur in men and women age 45 or older. Liver cancer is closely associated with hepatitis virus infections, especially hepatitis B.

A clinical trial, Hepatic Arterial Infusion of Melphalan with Hepatic Perfusion in Treating Patients with Unresectable Liver Cancer, is evaluating the effectiveness of hepatic arterial infusion (delivering chemotherapy directly to the liver) of the drug melphalan combined with hepatic perfusion (delivering chemotherapy to a blood vessel) in patients with liver cancer

The Etiology, Prevention, and Treatment of Hepatocellular Carcinoma program supports research on the etiology of liver cancer, development of animal models, novel prevention approaches, identification of reliable predictors of disease progression, and ways to minimize the morbidity and mortality associated with this disease.

The Tumor Microenvironment Network is exploring the role of the microenvironment, the cells and blood vessels that feed a tumor cell, in tumor initiation and progression. Network investigators are examining the role of inflammation and the microenvironment in the development of liver cancer.

ESOPHAGEAL CANCER

The Prevention Agents Program provides scientific and administrative oversight for chemoprevention agent development from preclinical research to early Phase I studies. The program is currently supporting research on several agents for potential chemoprevention of esophageal cancer.

The interdisciplinary scientists of the Network for Translational Research: Optical Imaging is accelerating translational research in optical imaging and/or spectroscopy. Current efforts include the development of techniques to identify molecular markers for detecting esophageal neoplasia and understanding basic disease mechanisms.

The Cancer Prevention Research Small Grant Program is supporting several research projects focused on esophageal cancer, including studies on esophageal cancer biomarkers, a mouse model of esophageal adenocarcinoma, and the molecular mechanisms involved in the development of Barrett esophagus. The latter is a condition in which the cells lining the lower part of the esophagus have changed or been replaced with abnormal cells that could lead to cancer of the esophagus. The backing up of stomach contents (reflux) may irritate the esophagus and, over time, cause Barrett esophagus.

LUNG CANCER

Lung cancer is the second most common cancer and the most common cause of cancer-related death in both men and women in the United States.

Seven lung cancer-specific Specialized Programs of Research Excellence (SPOREs) are promoting interdisciplinary research and moving basic research results from the laboratory to the clinical setting.

TCGA is assessing the feasibility of systematically identifying the major genomic changes involved in cancer using state-of-the-art genomic analysis technologies. Lung cancer is one of the first cancer types to be studied in the TCGA pilot phase.

PLCO Cancer Screening Trial is determining whether certain cancer screening tests reduce deaths from prostate, lung, colorectal, and ovarian cancers.

NCI's Lung Cancer Program supports research on early detection and treatment. The Lung Cancer Biomarkers Group is developing sets of specimens that can be used to test biomarkers for the early detection or diagnosis of lung cancer.

The Mouse Models of Human Cancers Consortium is developing models of lung cancer to aid in our understanding of lung tumor biology and to facilitate the development and testing of novel therapeutic approaches and methods for early diagnosis.

STOMACH CANCER

The overall incidence of stomach cancer in the United States has declined in the past 75 years. Five gastrointestinal cancer-specific SPOREs are moving results from the laboratory to the clinical setting.

The Tumor Microenvironment Network is exploring the role of the microenvironment, the cells and blood vessels that feed a tumor cell, in tumor initiation and progression. Network investigators are studying the role of inflammation and the tumor microenvironment in stomach cancer.

NCI's Infections and Immunoepidemiology Branch conducts high-impact epidemiologic research on infectious agents and cancer. Researchers are investigating why stomach cancer risk is low in Africa, despite high rates of Helicobacter pylori infection, as well as genetic factors associated with stomach cancer risk.

The Community Clinical Oncology Program (CCOP) and the Minority-Based Community Clinical Oncology Program (MB–CCOP) are comprehensive clinical trial mechanisms that disseminate the latest cancer prevention and treatment research findings to the community. Several CCOP and MB–CCOP groups currently participate in stomach cancer clinical trials.

MYELOMA

Myeloma, also known as multiple myeloma or plasma cell myeloma is the second most common blood cancer in the United States. The myeloma-specific SPORE is moving results from the laboratory to the clinical setting. This program is studying novel myeloma therapies and identifying new markers of this disease.

The Multiple Myeloma Prevention Study is evaluating the use of nonsteroidal anti-inflammatory drugs to modulate biomarkers associated with monoclonal gammopathy of undetermined significance, a condition that sometimes precedes the development of myeloma.

The Quick-trials for Novel Cancer Therapies and Prevention.—Exploratory Grants program expedites clinical translation of basic research discoveries in cancer biology through the development of novel anti-cancer drugs, diagnostic tools, treatments, and prevention strategies. This program currently supports two projects focused on immunotherapy and on improving the effectiveness of stem cell transplants in myeloma patients.

Question. Is NCI considering a plan to specifically and comprehensively address these lethal cancers?

Answer. Nearly half of the over 500,000 expected cancer deaths this year will be caused by 8 forms of cancer with 5-year relative survival rates of less than 50 percent-lung, liver, pancreatic, ovarian, brain, stomach, esophagus cancers and myeloma-and most of these cancers disproportionately affect minorities and under-

served subgroups in the United States. These cancers are often difficult to diagnose early. Cancers of high lethality pose a significant research challenge. These aggressive tumors are usually diagnosed late in their disease course, making the study of early disease progression and promotion, as well as the impact of genetic and environmental exposures, especially difficult.

NCI proposes to increase research on highly lethal cancers by expanding its investment into molecular epidemiological approaches such as the Cohort Consortium-of which the Pancreatic Cancer Cohort Consortium (PanScan) is one component—TCGA and genome-wide association studies to accelerate a fuller understanding of cancer causation and provide scientific direction of early detection, prevention and targeted therapeutic strategies. Molecular interrogation will generate data that can be used to evaluate profiles across the disease spectrum as well as among ethnic and racial populations.

NIH MEDLINE PLUS

Question. This subcommittee has long supported increased efforts by the NIH to provide the public important health information based on the results of the medical research their taxpayer monies support. At my urging, the NLM has increased its commitment to boost the distribution of the NIH MedlinePlus magazine. It is my understanding that a new bilingual version of the magazine, NIH MedlinePlus Salud, has been tested. What steps can be taken to substantially increase the public's access to these publications by getting them to all physician offices, community health clinics, and libraries?

Answer. Distribution of the magazines has increased from 50,000 copies of each issue in 2006 to over 500,000 copies of the English and Spanish versions in 2008. We estimate that the magazines now enjoy a readership of approximately 5 million nationwide. In February 2009, NLM created improved online versions of both magazines, which makes it easy for people to find, use, and email individual articles from the complete set of issues.

To increase distribution of the magazines still further, NLM, other NIH Institutes and Centers, and the Friends of the National Library of Medicine are forming partnerships with other Government agencies and private organizations which have an interest in supporting and enabling distribution of high-quality health information to their respective audiences. For example, the Peripheral Arterial Disease (PAD) Coalition supported the distribution of an additional 250,000 copies of one 2008 issue. In addition, the National Alliance for Hispanic Health is helping to support the production and distribution of NIH MedlinePlus Salud, which is an English/Spanish version. The pilot issue featured Cuban American journalist Cristina Saralegui, who is well known for her Univision talk show, The Cristina Show, as well as her work on behalf of health and wellness causes.

Question. Is this something that could be done with stimulus funding?

Answer. NIH is extremely grateful for the opportunities and funding provided in the American Recovery and Reinvestment Act of 2009 (ARRA) to preserve and create jobs and promote economic recovery by spurring technological advances in science and health. NLM is investigating how it may best use ARRA dollars to support the spirit of the Recovery Act, including increasing the distribution of the NIH MedlinePlus and NIH MedlinePlus Salud magazines.

INTERSTITIAL CYSTITIS

Question. According to NIH's recently revised methods for calculating support levels for various disease research areas, the amount dedicated to interstitial cystitis (IC) is less than half of what NIH previously believed it to be. (NIH originally estimated the fiscal year 2007 funding for IC research to be $23 million; new calculations show that the actual amount was just $10 million.) This is disappointing, given that this condition afflicts more than 8 million Americans.

What are the agency's plans to further basic and clinical research in this area?

Answer. NIH's shift to a new and more consistent process—requested by the Congress—to report on certain diseases and conditions through the Research, Condition, and Disease Categorization (RCDC) system, has indeed led to changes in reported funding levels for a variety of conditions, including IC. There are a number of reasons for these differences, including precise "definitions" for some disease reporting categories under the new system. More information is available on our RCDC Web site, at http://report.nih.gov/rcdc/reasons/. We began using RCDC to report actual funding levels in fiscal year 2008. To ensure transparency during the transition to RCDC, the NIH disease funding table provides a side-by-side comparison of the actual fiscal year 2007 levels produced using the prior method and the levels that would have resulted if RCDC had been implemented that year—thereby illustrating

the effect of the RCDC methodology and clarifying the changes between fiscal year 2007 and fiscal year 2008 resulting from use of this new process. For example, while the actual amount of funding reported for IC in fiscal year 2007 was $23 million, the RCDC analysis of the fiscal year 2007 portfolio reflected annual funding support of $10 million. The actual funding level reported for fiscal year 2008 of $10 million is comparable with the amount identified for fiscal year 2007 using the new RCDC methodology. While the impact of this change has in some instances resulted in significant one-time adjustments, it is important to note that they do not reflect a change in the NIH's commitment to research on IC and other conditions, and will ultimately result in more accurate, consistent reporting across NIH. Research that can lead to improved detection, treatment, or cure for IC remains a high priority for NIH.

QUESTIONS SUBMITTED BY SENATOR DANIEL K. INOUYE

PHARMACY PROGRAM

Question. Dr. Sidney McNairy, Director of the Division of Research Infrastructure, met with the University of Hawaii at Hilo faculty and administrative staff in December 2008. What are we doing or should we be doing to help the new University of Hawaii at Hilo's new pharmacy program meet the objectives set by Dr. McNairy's site visit?

Answer. One of the objectives set forth during Dr. McNairy's visit was to facilitate an expanded role of the University of Hawaii at Hilo in the Institutional Development Award (IDeA) Program's IDeA Networks of Biomedical Research Excellence (INBRE) initiative within National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH). The long-term objective is to facilitate the development of the research infrastructure in the School of Pharmacy at Hilo and foster collaboration with the Manoa campus.

Subsequent to this visit, Dr. McNairy and his staff set up several teleconferences with the Dean of the School of Medicine at the Manoa campus and the Dean of the School of Pharmacy at Hilo to discuss plans for the development of a joint application to compete for support via the INBRE initiative. As a result, these institutions are developing an application that includes core research facilities and instrumentation at the Hilo campus; support for research projects for junior faculty investigators at Hilo aimed at transitioning them to independent research support; and alterations and renovations at the Hilo campus. The Hawaii INBRE application will also include collaborations with several community colleges and 4-year institutions. Interactions with these latter institutions will provide the School of Pharmacy with an expanded pool of potential candidates for entry into the pharmacy program.

Question. What is being done to anchor these activities and help assure success?

Answer. NCRR staff participates in teleconferences with the Principal Investigator of the proposed Hawaii INBRE to review the details of the funding opportunity announcement (PAR–08–150), answer questions, and provide programmatic advice during the development of the application. The institutions are working toward the submission of this application in fiscal year 2009.

Question. Many initiatives and programs that have recently been launched by the National Cancer Institute (NCI) appear to be based on mechanisms that utilize center-based models. Large awards or cooperative agreements are made to large, well-established institutions and individual researchers. One criticism of such a model has been that it detracts from an already depleted investigator-initiated pool of grants for funding cancer and biomedical research. What steps is the NCI taking to ensure that adequate resources in the form of investigator-initiated research project grants continue to be made available to not only individual investigators but to young and/or new investigators?

Answer. The allocation to investigator-initiated research continues to represent the largest component of the NCI budget. That is a strong demonstration of the commitment the Institute has to investigator-initiated research. Equally strong is the Institute's commitment to first-time investigators. NCI allocated $74 million to pay new competing grant applications from first time investigators in fiscal year 2007 and raised that to $82 million in fiscal year 2008. Research Project Grants (RPGs) represent 44 percent of NCI's fiscal year 2009 budget. NCI intends to increase the number of first-time investigators in fiscal year 2009 using additional American Recovery and Reinvestment Act funds to support the first 2 years of their research project and then continuing their support in years 3–5 with appropriated funds.

INNOVATIVE APPROACHES AND NOVICE RESEARCHERS

Question. What efforts are currently underway to stimulate and support new, novel, and innovative approaches to the detection, treatment, and diagnosis of cancer?

Answer. NIH supports innovative approaches to the detection, treatment, and diagnosis of cancer. NCI established the Innovative Molecular Analysis Technologies (IMAT) program to support the development, technical maturation, and dissemination of novel and potentially transformative next-generation technologies through an approach of balanced, but targeted innovation. The IMAT program utilizes a variety of investigator-initiated research project grant mechanisms while retaining a strong commitment to diversity and to the training of scientists and clinicians in cross-cutting, research-enabling disciplines.

Nanotechnology represents a large number of advanced technologies that promise to change all aspects of 21st century medicine, especially cancer medicine. This is an area that brings scientists from physics, chemistry, mathematics, and engineering together with cancer biologists and oncologists to develop new cancer interventions. NCI launched the Alliance for Nanotechnology for Cancer program in 2004 to capitalize on these technologies. These centers are developing and translating novel nanotechnology-enabled diagnostic, imaging, and therapeutic platforms into clinical practice—which is required to capitalize on our prior investments in the molecular sciences. The original program produced several nano platforms that are currently in preclinical evaluation with a few already in clinical trials. The Alliance is a magnet for young creative scientists. Trained in the molecular sciences, bioinformatics, and physics, these centers have attracted the best—bringing Nobel Prize winners together with scientists that are early in their careers. Together they are creating new training and research opportunities that are driving this emerging field.

Question. Through what mechanisms are such programs funded, and is there a percentage or grant category designated to support the development of novice researchers?

Answer. NCI allocated 17 percent of the competing RPG budget to select grant applications that were identified as filling gaps in the research portfolio or representing novel approaches to research problems. We often refer to the grants funded with that pool as "exceptions" to the regular payline. One-third of that exception pool was allocated to supporting first-time investigators. Those exceptions are used across the portfolio, including in the areas of detection, treatment, and diagnosis.

The NCI Alliance for Nanotechnology in Cancer program, for example, utilizes several mechanisms, including the U54 center mechanism, R25 training center mechanism, K99/R00 fellowships mechanism, and U01 investigator-initiated research project mechanism. Based on comparison of landscape before and after the initial program, there is a clear trend of increased interest in cancer nanotechnology training as NIH fellowship applications supported by the original program (F32/F33) increased significantly since the program began. Postdoctoral students are the largest group participating in the alliance and, in fact, dominate the annual meeting where their research is presented. A similar increasing trend for NCI is seen in both individual training awards (K99) and institutional training awards (T32, R25). When the Alliance for Nanotechnology in Cancer began, the Institute supported a total of 4 individual-initiated grants in the field; that number has increased to 48 (excluding Alliance awardees) during the 5 years that the Alliance has been in place, and the Alliance shows signs of further expansion as more young people enter this new field.

MILITARY RESEARCHERS

Question. The National Institute of Nursing Research (NINR) lists (1) Integrating Biological and Behavioral Science for Better Health; (2) Adopting, Adapting and Generating New Technologies for Better Health Care; (3) Improving Methods for Future Scientific Discoveries; and (4) Developing Scientists for Today and Tomorrow as its 2006–2010 Strategic Goals, with a research emphasis on Promoting Health and Preventing Disease, Improving Quality of Life, Eliminating Health Disparities, and Setting Directions for End-of-Life Research. Historically, military nurse researchers have been unable to compete for funds due to the uniqueness of the population they serve. Considering the ongoing status of conflict in the Middle East and other countries, what efforts are being taken to allow military nurse researchers to actively compete for these funds?

Answer. The NINR strongly encourages all scientists to apply for funding within the NINR areas of research emphasis. There are no funding exclusions based on military status. Currently, the NINR is sponsoring a research initiative entitled,

"Improving Quality of Life of Patients and Family Following a War-Related Traumatic Injury" to develop and test personalized interventions to prevent complications in persons with war-related traumatic injuries during the post hospitalization transition period, with the ultimate goal of improving the health and quality of life of individuals and families following a war-related traumatic injury. NINR is actively involved in the collaboration between the NIH and the Center for Neuroscience and Regenerative Medicine at the Uniformed Services University of the Health Sciences (USHUS) to answer difficult research questions and improve medical care for service members with brain injuries and Post-Traumatic Stress Disorder. Through this collaboration, there are valuable training opportunities for nurse scientists. Other Federal partners collaborating in this effort are the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, Army Medical Research Command labs, Navy labs, and the Walter Reed National Military Medical Center.

NINR also has a long-standing relationship with the TriService Nursing Research Program at USHUS to facilitate collaboration and to consult on matters relevant to military nursing research. One of the members of the National Advisory Council for Nursing Research (NACNR) is Capt. Maggie Richard, Ph.D., MSN, NC, USN. Captain Richard is the director of the Human Research Protection Program in the Bureau of Medicine and Surgery, the Department of the Navy. She has served more than 20 years in the Navy Nurse Corps, and is the former head of the Nursing Research Service at the Bethesda National Naval Medical Center. As a member of the NACNR, Captain Richard provides the second level of review of grant applications, and recommends to the Institute Director which applications should be approved and considered for funding.

NINR remains dedicated to supporting clinical and basis research to help improve the health of the Nation, including members of the military service.

NCI AND CIS

Question. While the NCI intends to retain the information service arm of the Cancer Information Service (CIS) (i.e., 1–800–4CANCER service, the Internet, and instant messaging), NCI leadership has decided not to continue funding the CIS Partnership Program beyond the current contract period, ending January 15, 2010. What is NCI's plan for responding to the cancer information, training and technical assistance needs of remote, medically underserved communities and the organizations that serve them, such as those located in Hawaii and the U.S.-Associated Pacific Island jurisdictions?

Answer. Rather than renew the Partnership Program, we have reassessed how NCI can most effectively and efficiently disseminate important cancer information, and engage communities in order to realize an impact in the lives of those we serve. NCI will actively align its community outreach with its community-based research programs and build capacity in communities for the effective delivery of cancer information to their members. Building on the success of projects such as the Imi Hale-Native Hawaiian Cancer Network and the American Samoa Community Cancer Network, as well as the partnership between the University of Hawaii and the University of Guam, NCI will support community-based research programs that will build capacity to meet the needs of the underserved populations.

Beginning in January 2010, NCI will augment community-based research projects to include a community outreach structure that will specifically employ community outreach staff. While it is expected that these staff members will service the outreach needs for those funded projects, NCI is also expecting them to perform activities to address a broader area of needs identified by NCI. The funded projects that will initiate this new model of outreach include the Community Networks Program-II (CNP–II), the Minority Institution/Cancer Center Partnership (MI/CCP), and the NCI Community Cancer Center's Program (NCCCP), representing a total of 66 sites initially.

The establishment of a coordinated outreach network that works within established NCI-supported research programs will provide national geographic coverage for outreach to all populations. The proposed Community Outreach Core within the CNP–II concept will employ health education/community outreach staff to foster activities supporting the community and community partners. A similar approach within the MI/CCP and NCCCP would further augment and reinforce this national outreach network. Within the MI/CCP, for example, all partnerships are encouraged to have outreach programs and activities linking scientific discoveries and implementation of scientific breakthroughs in high-risk populations, and some partnerships are also increasing enrollment of racial/ethnic minorities in clinical trials. The outreach and partnership components of the CIS partnerships can be successfully

integrated and absorbed within the existing community outreach cores of NCI funded research initiatives to enhance and strengthen NCI's ability to educate and engage communities in addressing cancer health disparities within diverse, high-risk populations. NCI will also examine the feasibility of expanding this model to other NCI-funded programs.

NCI already has an outreach and dissemination infrastructure within its Office of Communications and Education that will provide these grantees the necessary technical assistance for communication, dissemination, and outreach. This infrastructure supports the current CIS Partnership Program. They are prepared to provide this national outreach network guidance in the use of best practices, the development of shared resources and tools, and the provision of training and technical assistance to community outreach coordinators in comprehensive cancer control and the delivery of evidence-based outreach activities.

In addition to the establishment of this national outreach network through NCI-funded programs, NCI is already in the process of planning a concept for dissemination, community outreach, and communication. This process, which has been described in responses to previous inquiries on this matter, utilizes a public health planning approach which examines the scientific evidence across areas of cancer control and engages the community throughout the process in feedback loops, and will ultimately yield a concept that aims to reduce the impact of cancer in the most vulnerable communities. Greater details on the planning process for this can be provided upon request.

QUESTION SUBMITTED BY SENATOR HERB KOHL

INCREASING FUNDING AND GREATER NUMBER OF AWARDS

Question. Dr. Kington, I was pleased to see that funding sources for the National Institutes of Health Clinical and Translational Science Awards (CTSA) were increased this year, through both the fiscal year 2009 omnibus appropriations bill and the American Reinvestment and Recovery Act. I am aware that several institutions applying for awards this year, including applicants in my home State of Wisconsin, have received "outstanding" application ratings. Will this increase in funding allow for a greater number of awards to be distributed?

Answer. The funding provided in the Omnibus Appropriations Act, 2009, will support new CTSAs in fiscal year 2009 as the program moves closer to a goal of 60 CTSAs.

The American Recovery and Reinvestment Act (ARRA) funding is being used to allow existing CTSAs to compete for resources to supplement their current activity, plus support other researchers who may apply to leverage current CTSA activities. However, since normal CTSA funding is for 5 years and ARRA funds are limited to 2 years the funding is not able to support new awards.

QUESTIONS SUBMITTED BY SENATOR MARY L. LANDRIEU

SMALL BUSINESS INNOVATION RESEARCH (SBIR) AND SMALL BUSINESS TECHNOLOGY TRANSFER (STTR) PROGRAMS

Question. When the American Recovery and Reinvestment Act (ARRA) passed in February, it contained a short sentence that directly hurt small businesses by exempting two important small business programs. The provision, which provided $8.2 billion to the National Institutes of Health's (NIH), exempted the NIH from the statutory requirement that 2.8 percent of extramural research and development (R&D) money be used for the Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) programs. As the chair of the Senate Small Business Committee, and as a member of this appropriations subcommittee, I was never consulted or notified about the exemption language which was added in conference. My staff has been told by NIH officials and others that NIH directly requested the exemption. As a result of the exemption, the NIH is not required to award up to $200 million from the ARRA funds to small businesses for research and development. This exemption went directly counter to the principles and goals of ARRA. The recovery effort was supposed to be about creating high-quality jobs, spurring innovation, and giving a boost to businesses across the board. Instead, this language singled out small businesses and slashed the relatively tiny amount they are normally guaranteed. I have several questions for Dr. Kington regarding NIH's request and the exemption: Specifically, who at the NIH requested that ARRA be

exempt from funding the SBIR and STTR programs? Was this request first cleared through you?

Answer. NIH was concerned about the decreasing number of SBIR applications. We had seen nearly a 40 percent decrease in applications during the fiscal years 2004 through 2008. Although the NIH is not required by this law to provide a set amount of ARRA funds toward the SBIR/STTR programs, it is important to note that small businesses are able to apply for and will receive funds. NIH remains committed to the small business community and has been encouraging small businesses to apply for stimulus funds through various funding opportunity announcements that have been released.

Question. From your experience at NIH, would you agree that the SBIR and STTR programs play a vital role in NIH's extramural R&D because of the high levels of innovation that come out of these two programs?

Answer. NIH has supported and continues to support small business and efforts to bring innovations from biomedical research to the taxpayer. NIH research is driving a vibrant community of American small businesses and entrepreneurs in the health enterprise. NIH-funded research leads to patents and spin-off companies across the Nation. Through the SBIR and STTR programs, the NIH helps nurture entrepreneurs as they bring products to the international market that improve health and well-being. Small businesses supported by NIH grants help maintain American economic leadership.

For example, Kinetic Muscles, a small business in Arizona, has developed the Hand Mentor ProT, which is a device designed for neurological rehabilitation of the hand and wrist for people who have suffered strokes or other brain injuries. In partnership with their exclusive distributor, Columbia Scientific, the Hand Mentor ProT is now being used in select HealthSouth rehabilitation hospitals.

Biopsy Sciences of Florida has developed the Bio-SealT and recently sold the technology to Angiotech Pharmaceutics, Inc. (a global specialty pharmaceutical and medical device company). This novel technology was designed to reduce the incidence of postoperative pneumothorax (collapsed lung) in patients who undergo lung biopsy procedures. The technology involves placement of an expanding hydrogel plug along the biopsy needle track during the procedure, closing off the track to subsequent influx of air into the chest during respiration after the biopsy needle is withdrawn. The seal is airtight and the plug is absorbed into the body after healing of the puncture site has occurred.

These are only a few examples of the high level of innovation and the many products that have been developed with NIH SBIR/STTR funding.

Question. From your experience at NIH, would you agree that small businesses doing extramural R&D for the NIH have a proven record of creating jobs?

Answer. Small businesses have long been the engine of U.S. economic growth, generating a significant proportion of new jobs annually, and we believe NIH's SBIR/STTR programs assist with the creation of high-quality jobs. NIH has invested in excess of $5 billion in more than 19,000 projects to over 5,000 small businesses. Past studies of the SBIR program conducted by the NIH and the National Research Council (NRC) have shown small businesses are seen as sources of economic vitality and are especially important as a source of new employment.

Question. Could you please provide, in detail, the steps NIH is taking to make sure small businesses receive an adequate share of ARRA funds?

Answer. NIH has taken several steps to ensure small businesses receive an adequate share of the ARRA funds appropriated to NIH. Outreach efforts have been stepped up to alert small companies of ARRA opportunities. In the last few months, eight SBIR/STTR presentations have been given throughout the country at life science or SBIR/STTR conferences in New Jersey, Indiana, Kentucky, New York, Maryland, Washington, DC, and California. NIH's 11th Annual SBIR/STTR Conference was held at the end of June 2009 in Omaha, Nebraska, and with attendance typically in the hundreds, this was another excellent opportunity to disseminate information about specifically targeted ARRA opportunities to this small business audience.

During the past few months, NIH has strongly encouraged small businesses to apply for several of its funding opportunity announcements (FOAs) that were supported by ARRA, including:

—The NIH Challenge Grants in Health and Science Research or "Challenge Grants" http://grants.nih.gov/grants/guide/rfa-files/RFA–OD–09–003.html

This opportunity focuses on specific knowledge gaps, new technologies, data generation, or research methods that would benefit from an influx of funds to quickly advance the area in significant ways.

—Research and Research Infrastructure "Grand Opportunities" or "GO Grants" http://grants.nih.gov/grants/guide/rfa-files/RFA–OD–09–004.html

This opportunity focuses on developing and implementing critical research innovations to advance their research enterprises, stimulate future growth and investments, and advance public health and health care delivery.

In June, NIH released two additional announcements that explicitly targeted the private sector commercial research community. These included:

—Recovery Act Limited Competition: Biomedical Research, Development, and Growth to Spur the Acceleration of New Technologies (BRDG–SPAN) Pilot Program, http://grants.nih.gov/grants/guide/rfa-files/RFA–OD–09–008.html

This FOA is a pilot program that focuses on the funding gap between promising research and development and transitioning to the market by contributing to the critical funding needed to pursue the next appropriate milestone(s) toward ultimate commercialization. Any U.S.-owned, for-profit enterprise/commercial organization is encouraged to apply for this funding. Please note that applications received under this FOA may be given funding priority if the applicant is associated with an enterprise or commercial organization that is of small size and/or has limited resources.

—Recovery Act Limited Competition: Small Business Catalyst Awards for Accelerating Innovative Research, http://grants.nih.gov/grants/guide/rfa-files/RFA–OD–09–009.html

This opportunity specifically targets the SBIR research community and focuses on accelerating innovation through high- risk, high-reward research and development that has commercial potential and is relevant to the NIH mission. It seeks to encourage fresh research perspectives and approaches and focuses on early-stage ideas that promise to lead to major leaps forward rather than incremental improvements of existing technologies. Only U.S. small business concerns are eligible to submit Phase I SBIR applications, and first-time applicants to NIH may receive funding priority.

In addition to releasing these funding opportunity announcements, the pay-lines at various NIH Institutes and Centers have been extended to reach more meritorious research grants, including those submitted by small businesses. Finally, in March 2009, NIH offered three administrative supplement and competitive revision opportunities for those with active research project grants (including SBIR and STTR). The supplements provided additional funding to accelerate the tempo of scientific research on active grants. Revision awards support a significant expansion of the scope or research protocol of approved and funded projects. Administrative supplements were also offered to provide summer research experiences for students and science educators. SBIR and STTR projects successfully competed. At this time, over 20 SBIR/STTR grantees have been selected to receive administrative supplements to provide summer research experiences for students and/or science educators.

Question. My staff has been told by NIH officials that you are setting up a Pilot program for small businesses with your discretionary ARRA funds. Can you please report to the Senate Small Business Committee on the nature and progress of this Pilot program?

Answer. You are correct, NIH recently announced the ARRA-funded BRDG–SPAN Pilot Program to focus on the gap between research and development and transitioning to the market.

Only U.S.-owned for-profit enterprise/commercial organizations may apply, and although not explicitly limited to small businesses, most of the applications are expected to be submitted by small businesses. Applications received under this funding opportunity may be given funding priority if the applicant is associated with an enterprise/commercial organization that is of small size and/or of limited resources.

In addition, we have another ARRA-funded small business program called the Catalyst Awards, and only U.S. small business concerns are eligible to submit SBIR applications.

Question. I have looked at a number of legislative vehicles, including the fiscal year 2010 Labor HHS Appropriations bill, to make up for the loss of money to small businesses that was created by the small business exemption in ARRA. Can you give me your thoughts on how this money can be made up, whether it be legislatively or through proactive actions by the NIH?

Answer. NIH's current commitments to small business research instill confidence that this research community will receive a fair portion of NIH's extramural funding. This is already in evidence, since a large number of applications were received from small businesses in response to our initial ARRA-supported FOAs, and applications are still being received from small businesses in response to ARRA FOAs that remain open.

QUESTIONS SUBMITTED BY SENATOR ARLEN SPECTER

MATERNAL FETAL MEDICINE RESEARCH NETWORK

Question. I am aware of the critical research conducted by the National Institute of Child Health and Human Development (NICHD) Maternal Fetal Medicine Research Network in the area of preterm birth and maternal complications. What are your plans for this Network in the fiscal year 2010 budget?

Answer. The Maternal Fetal Medicine Units Network (MFMU) is one of the landmark research networks within NICHD. Conducting research that may affect pregnant women and their offspring can present some critical health and ethical issues. Yet improvements in clinical practice and care are dependent on evidence-based research, and the Network was created in response to this need. This research mechanism permits large-scale clinical studies that provide the necessary information to allow healthcare professionals to translate the findings into everyday clinical practice.Specifically, the MFMU Network conducts clinical trials and observational studies in obstetrics to improve maternal and neonatal outcomes. It is essential for each Network participant to conduct this work in the same manner (i.e. following the same protocol) in order to have comparable results that can be applied across the Nation and for different population groups. In addition, preventive measures and interventions can be tested to find out if they work, or just as important, if they do not.

NICHD has spent approximately $170 million since the MFMU Network's inception in 1986. It is re-competed every 5 years to ensure that only the best scientists are funded to do this work. The existing network will expire in fiscal year 2011. The networks scientific success supports considering a new competition in fiscal year 2011. As is typical, decisions regarding extending the Network will be made during development of the 2011 budget. Current projections for fiscal year 2010 are $12.6 million in NICHD funding. Along with a projected $700,000 contribution from NINDS in fiscal year 2010, the total support level comes to $13.3 million.

SALIVARY DIAGNOSTICS

Question. Dental schools, and I have one in my State, are doing some rather exciting research in the area of saliva as a diagnostic tool. Where does this research stand at this point?

Answer. Saliva is a complex mixture of water, antibodies, and other specialized protective proteins, important for maintaining oral health, function, and comfort. It has long been recognized that saliva acts as a mirror of the body's health, in that it contains the full repertoire of proteins, hormones, antibodies, and other substances that are frequently measured in standard blood tests to monitor health and disease. Saliva is easy to collect, even repeatedly if needed, and poses none of the risks, fears, or invasiveness of blood tests.

Saliva has already been used reliably to detect a number of diseases, including HIV, as well as viral hepatitis A, B, and C. It also can be used to monitor a variety of drug levels, including those of marijuana, cocaine, and alcohol. The National Institute of Dental and Craniofacial Research (NIDCR) is supporting efforts to identify and validate biomarkers, and to also support technology to overcome barriers to the widespread use of salivary diagnostics. For example researchers are focused on developing microchip assays for point-of-care delivery, and are making impressive progress at achieving high-sensitivity, high-specificity, miniaturization, automation, portability, low cost, speed, and the ability to assay a large number of samples and biomarkers concurrently.

Last year, scientists funded by NIDCR completed the first full catalogue of proteins present in saliva. This protein dictionary will serve as an essential reference point as scientists continue to validate saliva as a diagnostic fluid. This resource also complements our growing ability to leverage DNA and RNA as biomarkers. For example, in October 2008, NIDCR-supported scientists reported that they could use a panel of 5 RNA biomarkers to accurately detect oral squamous cell carcinoma, a form of oral cancer, more than 90 percent of the time.

Question. Is progress being made?

Answer. Yes, progress is being made. The field of salivary diagnostics combines the power of mathematics, biology, genomics, proteomics, engineering, computer science, and other areas, with the goal of using saliva as a diagnostic fluid for a variety of conditions, from AIDS to cancer to diabetes. Several NIDCR grantees are now working to develop and assemble tiny "labs on a chip" that can precisely measure levels of the various antibodies, antigens, and nucleic acids present in saliva, all of which may indicate a developing disease or condition. In contrast to existing blood tests which require painful needle sticks, salivary tests could be performed on

the spot and rapidly scan oral fluids for the presence or absence of multiple proteins linked to various systemic diseases and conditions. NIDCR is currently supporting the development of devices that will detect infectious diseases, cancer, renal diseases, steroid hormones, and inflammatory markers for cardiovascular and pulmonary diseases. The technologies being developed also will be effective for tracking new, as-yet unidentified biomarkers.

As an illustration of progress in this area, NIDCR scientists recently reported clinical success in detecting C-reactive protein in human saliva with an ultrasensitive microchip assay system. C-reactive protein, a serum protein indicative of inflammation, is elevated in people with periodontal disease and may be predictive of developing heart disease.

Question. Will we be able to go to our dentist and undergo this noninvasive diagnostic test to detect early markers of diseases, such as Alzheimer's disease, pancreatic, and breast cancer?

Answer. This is part of our vision for the future; saliva is easy to collect and poses none of the risks, fears, or invasiveness of blood tests. The miniaturization of detection devices may allow placement of the sentinel device directly in the mouth, yielding real-time surveillance of hundreds of biomarkers that could alert individuals to consult with their health professionals at the earliest moment of disease, or to monitor the progression and recurrence of diseases in patients undergoing treatment. This will enable oral healthcare professionals to assume a more prominent role in primary care and disease prevention that will assume increasing importance as the American population ages. NIDCR will continue to support ongoing studies, as well as new studies including those made possible by American Recovery and Reinvestment Act funding, that will examine the feasibility of developing salivary diagnostic testing for the early markers of a number of diseases, including Alzheimer's disease and several cancers. The recent success of NIDCR-supported researchers in identifying salivary markers for primary Sjögren's syndrome, a chronic autoimmune condition of the salivary and tear glands that affects about 2 million Americans, mainly women, is another example of progress in this area.

Salivary diagnostics could have benefits far beyond medicine and dentistry as well. For example, law enforcement agencies could employ saliva tests both forensically and in the field to determine rapidly whether a person is intoxicated or has recently used illegal drugs. These tests may also be beneficial in determining exposures to environmental, occupational, and biological substances, such as anthrax.

NIH BUDGET WITH PRESIDENTIAL INITIATIVES

Question. The budget presented provides an increase of $174 million for all research except cancer. Will this essentially flat budget funding be sufficient to meet the important research work being conducted by the National Institutes of Health (NIH)?

Answer. We believe that the fiscal year 2010 NIH funding priorities are sound and will ensure the rapid translation of science from the laboratory to the bedside. The budget supports more than 9,800 competing Research Project Grants in addition to exponentially funding cancer as an initiative.

NIH's research categories are not mutually exclusive and individual research projects can be included in multiple categories as in cancer research; we have seen progress in one disease often comes from unrelated areas of investigation, and through the mutual synergy of such research that transformational findings occur. NIH will continue to fund high-quality research in all areas of its portfolio and will continue to effectively use every resource we receive in support of biomedical research.

STEM CELLS

Question. What do you think is necessary in terms of time and funding to make research breakthroughs in stem cell research?

Answer. The NIH has been clear that the best way to make breakthroughs in stem cell research is to pursue all avenues of stem cell research simultaneously as: (1) it is impossible to predict which type of stem cell research (e.g., adult or human embryonic) will ultimately yield the most successful approach in any given stem cell application; and (2) work in both adult and embryonic stem cells continues to inform and facilitate progress in stem cell research.

It is difficult to predict a timeline for scientific breakthroughs or determine a budget that will achieve these breakthroughs for stem cell research or any other type of research. Since 2001, NIH has been the lead Federal agency supporting and conducting human embryonic stem cell (hESC) research, spending over $262 million

on hESC research during this period. This research has significantly enhanced our understanding of the basic biology of these unique cells. For example, the genes required for maintaining pluripotency were determined by studying hESCs which led in 2007 to the breakthrough discovery of human-induced pluripotent stem cells. These cells are now being studied along with adult and hESCs to elucidate the unique characteristics and potential uses of each cell type.

As you are aware, President Barack Obama signed Executive Order 13505 on March 9, 2009, which requires NIH to establish new guidelines for Federal funding of human embryonic stem cell (hESC) research. NIH will issue the final guidelines by July 7, 2009. These new guidelines should increase ethical oversight and the number of responsibly derived hESC lines eligible for Federal funding. We anticipate that NIH will be able to provide support for research using many new hESC lines that were not previously eligible for Federal funding. It is our expectation that the expansion of the number of human embryonic stem cell lines available to scientists funded by NIH will hasten stem cell breakthroughs.

As you know, there has never been a cap on how much NIH could potentially spend on stem cell research, adult or embryonic. Instead, the amount spent depends on the number of highly meritorious stem cell grants that are submitted by the scientific community. The scientific community has told us about additional research that will be enabled by the increase in the number of human embryonic stem cell lines eligible for Federal funding that will result from the new policy. Once the new Guidelines are in place, NIH will assess the research needs and opportunities in stem cell biology and will develop initiatives that meet those needs to capitalize on these opportunities.

LOWER Lp(a)

Question. Several years ago, I asked Dr. L'Enfant about your research for a medication to lower Lp(a). Is there anything new that you can tell me about the status of research toward a medication that lowers Lp(a)?

Answer. Of all the drugs we currently use to treat abnormal lipoproteins, the one that most consistently lowers Lp(a) levels is a drug that has been around quite a while—niacin. Although the National Heart, Lung and Blood Institute (NHLBI) does not ordinarily sponsor drug development, as that is the province of the pharmaceutical companies, we are currently supporting a very important randomized clinical trial called AIM–HIGH. The trial is testing whether an extended release form of niacin (Niaspanr) will improve outcomes in 3,300 patients who have cardiovascular disease and "atherogenic dyslipidemia," a fairly common constellation of lipoprotein abnormalities associated with high cardiovascular risk that often includes high Lp(a) levels. We have funded an ancillary study to the AIM–HIGH trial specifically to learn more about how niacin affects lipoproteins, including Lp(a), and to determine the extent to which the effects may explain any observed improvement in cardiovascular outcomes. The information this study will provide about the role of Lp(a)in cardiovascular disease may help inform subsequent drug development efforts.

CURING CANCER

Question. The cancer community has indicated that $335 billion over the next 15 years is necessary to make real progress toward cancer cures. What do you think is necessary in terms of time, funding, and research breakthroughs to make a real difference in curing cancer?

Answer. The National Cancer Institute (NCI) is currently working with the other Institutes and Centers at NIH to develop an NIH cancer research strategic plan for the proposed plan by President Obama to double cancer research funding over the next 8 years. The strategic plan recognizes that most advances in the field will be made because of the knowledge that cancer is a disease of genomic alterations and of tumor cell evolution.

The NCI is developing a personalized cancer care platform—based upon the knowledge that cancer is a disease of altered genes—that will encompass and enable a drug development platform, from discovery of genetic changes to translation to man. Advanced genome sequencing technology will soon make it possible to completely sequence both normal and disease tissue of individual patients. NCI is developing a comprehensive approach to translate raw genetic information into an intimate understanding of the function of the genetic pathways which can then be used to clearly define targets for manipulating those pathways to inform the development of new targeted interventions. NCI is taking steps to create the first of a small national network of tumor characterization centers that will match a genetically characterized patient's tumor to appropriate and optimal therapeutic solutions. This 21st

century vision for personalized medicine will connect individuals, organizations, institutions, and the concomitant information in a cycle of discovery, development, and clinical care.

As the leader of the National Cancer Program, NCI is building on its history of research success and wisely spending every dollar it receives in a continual effort to foster the best research and to connect the public, private, and academic sectors for effective translation of these discoveries. With the significant funding increases proposed by the President, NCI could realize the promise of personalized cancer care more rapidly by significantly shortening the path between making an innovative discovery in the laboratory to having an effective impact on a patient in the clinic.

In this new era of post-human-genome science, it is clear that multiple new agents will be necessary to target multiple cancer pathways in each unique patient. Small molecules will penetrate cancer cells. New agents will energize the body's immune system to fight tumors. Still other agents will target the seemingly normal tissue of the tumor microenvironment or the tumor initiator cells with "stem-like" characteristics that may lead to cancer's deadly spread. Consequently, we will need to continue to expand discovery of the underlying genetic signatures of cancer and to develop individual recipes of therapy, often using multiple drugs from multiple manufacturers.

It is in the area of developing orphan drugs or combination therapies where industry—concerned about marketability, intellectual property, competition, and liability issues—often fears to tread. NCI must fill that void:

—Through increased funding of the Developmental Therapeutics Program and other allied programs, NCI could greatly expand a cohesive effort to produce small quantities of new agents and begin first-in-human testing, which would, in turn, lead to commercialization at a more rapid pace.

—Through a well-financed, coordinated plan, NCI could importantly restructure how it conducts clinical trials, creating an electronically connected system capable of bringing early phase clinical research to millions more patients, in their home communities.

—Through strategically placed characterization centers, NCI could conduct the intensely technological and specialized testing necessary in an era of targeted agents. This effort could create the standards of tumor analysis required in this new age, and could more effectively address the demands of rapidly changing technology. Examples of needed programs include early phase pharmacodynamic studies, a U.S. oncology tissue bank and certified centralized tumor characterization laboratories.

—Additional development of advanced technologies will allow us further develop nanoparticles designed to penetrate tumors and conduct greater research into the telltale proteins in the body that could be used to enhance early diagnosis. Enhancing technology development in clinical proteomics, systems biology, and increasing our biomedical computing capabilities would accelerate progress against cancer, but could also be applied to understanding other diseases.

—Through greater development of imaging, science could refine and improve the capacity to look inside cells, revealing biological processes in real time. This effort could develop the next generation of tools for early diagnosis, at a time when there are only a few million cancer cells in a patient's body.

QUESTIONS SUBMITTED BY SENATOR THAD COCHRAN

SARCOIDOSIS

Question. Sarcoidosis is a systemic inflammatory disease and one of the most common causes of fibrotic lung disease in the United States. Sarcoidosis can cause chronic debilitating or life-threatening heart, neurological, and internal organ disease and has no safe, effective treatments. In North America, African Americans are about five times more likely to have sarcoidosis than whites, representing a significant national health disparity. Despite the substantial burden of this illness on many (tens of) thousands of Americans of all races, and significant recent progress in our understanding of the illness, the National Institutes of Health (NIH) has supported disproportionately little research for this disease relative to its burden of disease, a disparity that has been increasing over the past decade. What do you believe are the reasons for this disparity and how can it be corrected?

Answer. The National Heart, Lung and Blood Institute (NHLBI) has had a longstanding commitment to funding research on the causes and treatment of sarcoidosis and on genetic predisposition to developing it. In recent years the Institute developed several new initiatives specifically addressing sarcoidosis, including a solici-

tation on granulomatous inflammation in sarcoidosis that resulted in funding of 11 new research projects. The Institute currently supports exciting programs in genomics of sarcoidosis and a new clinical trial on atorvastatin as a disease-modifying agent in pulmonary sarcoidosis. One reason for the funding disparity may be the small numbers of investigators in the country who are interested in conducting research in this complex and multi-organ disease. In addition, applications submitted have not competed well. Some steps we are taking to address this disparity include increasing visibility of sarcoidosis through activities such as radio spots on the disease; developing new research initiatives to address specific aspects of the disease; and working with the Trans NIH Sarcoidosis Working Group, which coordinates sarcoidosis research activities across the NIH. One of its recent activities has been promotion of a workshop on the genetics of sarcoidosis that was held last summer. Workshop recommendations, which have been posted on the NHLBI Web site, include initiation of a community-based study of sarcoidosis that would develop a registry of clinical information about the disease and might also include collection of patient samples for genetic studies. Other recommendations were to promote collaboration on sarcoidosis with NHLBI-funded investigators and the scientific community in Europe and other parts of the world, and to launch a genome-wide association study (GWAS) based on available samples from ACCESS and other existing cohorts. NHLBI staff are following up on these recommendations. Via the NIH solicitation for Challenge grants under the American Recovery and Reinvestment Act (ARRA), the NHLBI requested GWAS on rare lung diseases, including sarcoidosis.

Question. What are the plans of the NHLBI for closing this gap and improving the clinical care and treatment for patients with sarcoidosis?

Answer. Our plan is to support ongoing and new meritorious research through both ARRA and traditional investigator-initiated applications; re-issue an NIH-wide sarcoidosis program announcement, which seeks to stimulate research on the multi-organ manifestations of the disease; continue support of the NHLBI atorvastatin clinical trial; and consider future initiatives based on the NHLBI workshop on genetics of sarcoidosis that was held last summer. A new initiative under consideration addresses cardiac dysfunction associated with sarcoidosis. We are optimistic that these efforts will lead to advances in understanding the origin and pathogenesis of this disease and will improve our ability to diagnose and treat affected individuals.

QUESTIONS SUBMITTED BY SENATOR RICHARD C. SHELBY

CLINICAL AND TRANSATIONAL AWARDS

Question. The Clinical and Translational Science Awards (CTSA) is designed to transform how clinical and translational research is conducted, ultimately enabling researchers to provide new treatments more efficiently to patients. Tremendous effort has brought institutions together to rally around this program, yet current funding levels make it difficult for the programs to succeed. Key to the success of the CTSA is the development of cost sharing for use of infrastructure services. An example of this mechanism is the General Clinical Research Centers (GCRC), which allowed institutes to reduce their research budgets by having investigators use the GCRC when clinical care such as inpatient stays, lab tests, and nursing staff was made available at no additional cost. Today, individual investigators must provide funds for clinical care cost sharing from grants funded from other National Institutes of Health (NIH) Institutes. As research becomes more expensive and private capital dries up, it becomes even more critical to ensure support for translational research, that is, research that moves a potential therapy from development to the market. Will the NIH provide the financial resources necessary to maximize the potential of this critical program?

Answer. The CTSA program is providing substantially more funding for clinical research than was available under the GCRC program. The CTSA allows the institution to continue activities that were conducted in the GCRC and add new activities. With a minimum total funding level of $4 million per year, all CTSAs will be able to offer clinical investigators a substantial diversity of resources. The prioritization of resources offered within an institution is determined locally, as are any needs for cost sharing to ensure adequate support for a wide range of activities.

National Center for Research Resources (NCRR) expects to fulfill the charge to transform clinical and translational research within the current overall budget for the program. At $500 million per year when fully implemented, the CTSA program represents a significant increase in infrastructure support over the $340 million allocated to pre-existing NIH clinical research resources (i.e., NCRR K12, GCRC M01,

NIH K30, and Roadmap T32 and K12 programs). To reach the critical mass necessary to transform clinical and translational research, NCRR projects that 60 CTSAs are needed throughout the United States. Diversity in the size, scope, and geographic location of participating institutions will strengthen the CTSA consortium and enhance its national and regional collaborations

CONCLUSION OF HEARINGS

Senator HARKIN.So again, I thank you all very much, and with that the subcommittee will stand recessed.

Dr. KINGTON. Thank you.

[Whereupon, at 11:49 a.m., Thursday, May 21, the subcommittee was recessed, to reconvene subject to the call of the Chair.]